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Vol. XII, No. 7 JULY, 1923

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

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Published Monthly by the American Pharmaceutical Association: Office of Publication, 211 Church St., Easton, Pa. Editorial Office, 253 Bourse Building, Philadelphia, Pa. Annual Subscription, $4.00; Single Numbers, 35 Cents.

THE SEVENTY-FIRST ANNUAL CONVENTION OF THE AMERICAN PHARMACEUTICAL ASSOCIATION WILL BE HELD IN ASHEVILLE, N. C., DURING THE WEEK OF SEPTEMBER 3, 1923.

The 1923 meetings of the American Conference of Pharmaceutical Faculties and the National Association of Boards of Pharmacy will also be held in Asheville during the week of September 3.

For Association Roster see pages x, xii, xiv, and xv.

Entered as Second-class Matter, January 23, 1917, at the Post Office at Easton, Pa., under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103. Act of October 3, 1917, authorized July 10, 1918.

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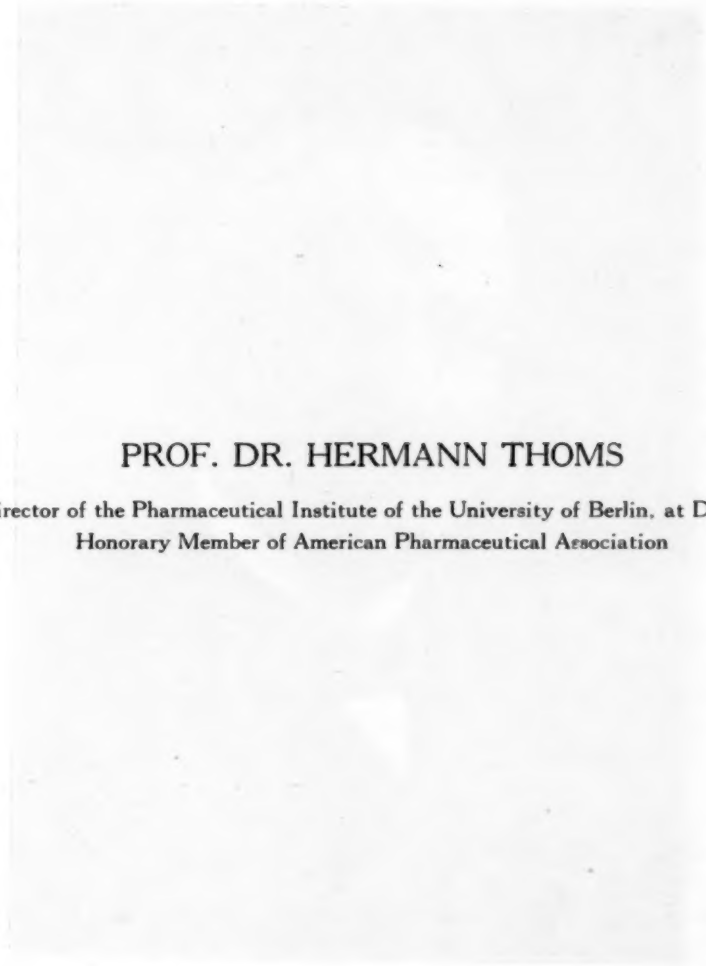
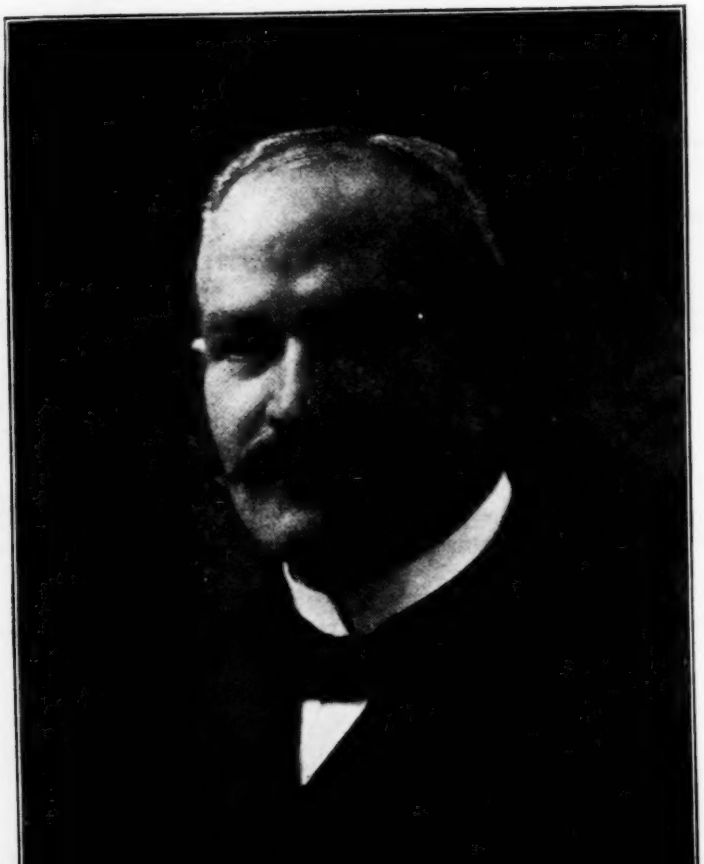


PROF. DR. HERMANN THOMS

Director of the Pharmaceutical Institute of the University of Berlin, at Dahlem.
Honorary Member of American Pharmaceutical Association



HERMANN THOMS.

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XII JULY, 1923 No. 7

HERMANN THOMS.

The American Pharmaceutical Association is to be congratulated upon its having buried the "hatchet" and having elected such a man as Professor Thoms of Berlin an honorary member. While we take keen pleasure in commending our oldest national organization on its action so soon after the war, a sense of sorrow mingles with our pleasure when we recall that this action was impossible in March 1919 when Professor Thoms' sixtieth birthday was remembered in more than one European country.

In honoring Professor Thoms, the A. Ph. A. has done more than to pay tribute to an individual. Scientific pharmacy possibly owes a greater debt to Germany than to any other country. Even while Germany was but a geographic conception, pharmacy, like chemistry, flourished on German soil. Book literature and journals reveal the extent of the progress made. Many an American pharmacist went to German universities for a year or two to complete his scientific education and after his return to this country implanted upon American soil some of that love for the advancement of our science so characteristic of his teachers.

Yet with all this progress, the University of Berlin was for a long period without a real home for pharmacy. Men whose names are well known to the scientific world had lectured on pharmaceutical subjects, but they were associated with either chemistry or botany. Only recently we had occasion to read in Tschirch's own words (*Erlebtes und Erstrebtes*) how this enthusiast for pharmacy had attempted to create a pharmaceutical center in Berlin, but that he had not succeeded. Possibly it was Tschirch's leaving for Bern that roused German pharmacy and made it possible for Thoms to succeed in establishing the foremost scientific institute for pharmacy at the German capital. Aided though he may have been by Tschirch's failure, he had no easy task. His life-work consisted as much in overcoming obstacles as in rearing a structure that may well serve as a model the world over.

While the collected "Arbeiten aus dem Pharmaceutischen Institut," which should not be wanting in any college library of this country, are a monument to the scientific energy of the staff, of which he was the inspiring leader—an energy

which was not seriously impaired even during the trying years of the war—his efforts reached out farther than the German capital and its university. The Deutsche Pharmaceutische Gesellschaft, the "Berichte" of which should likewise be on the shelves of every college library, is essentially his creation. These two instances must suffice to illustrate the general activities of the man. Suffice it to add that, with Professor Moeller, he edited the volumes of the second edition of the "Real-Encyclopaedie der gesammten Pharmacie." How any college library can make any pretense at being a pharmaceutical library without this masterpiece of pharmaceutical encyclopedias calls for a special explanation.

The American Pharmaceutical Association has honored itself by honoring this man and all that he represents. However, we have honored ourselves primarily in not allowing war hatred to interfere with the long-merited recognition. But, are we going to stop here? German students are working in coal mines in order to pay their way through the university. German professors may have meat on their table once a week and be grateful. Neither the menial labor which the students perform nor the semi-starvation diet of the teachers seemingly interferes seriously with either studies or investigation. But when a single reagent is so high priced as to be beyond the student's means, when the professor no longer can afford a research assistant, when the income of the institute makes the purchase of foreign journals absolutely impossible, then it is time to remind the members of the A. Ph. A. of the motto on the Flueckiger medal:

Scientia non est unius populi sed orbis terrarum

True, we are doing none too much for our own scientific institutes, but this should not make us unmindful of the crying needs of pharmaceutical science as represented in that country which has done so much for the uplift of our calling and of which country Professor Thoms is one of the principal living representatives. To our calling Professor Thoms has devoted a long and busy life. Appreciation, no doubt, is dear to his heart, but, I am certain, he will find greater satisfaction to see German scientific pharmacy assisted in this hour of greatest need, than to have volumes of flattery showered upon him.

Almost immediately after having penned these words, the writer received a letter from Professor Thoms stating that his Japanese friends have invited him to visit their country. On his way to Japan, Professor Thoms will cross our continent and will stop at several pharmaceutical centers. Thus the opportunity is unexpectedly extended to us to show that we are no less appreciative of one of the foremost representatives of scientific pharmacy than are our Japanese colleagues; if these can make a present of a trip around the world to their former teacher, what will the pharmacists of the United States do to show themselves at all worthy of their Teacher?

EDWARD KREMERS.

JULY 1923.

THE EFFICIENCY OF HYDRATED OXIDE OF IRON AS AN ANTIDOTE FOR ARSENIC.

To the Editor, Journal A. Ph. A.:

Dr. Horatio C. Wood objects to our conclusions that freshly precipitated ferric hydroxide is of no practical value in the treatment of arsenical poisoning, and quotes our own figures to prove the contrary. We were fully cognizant of the value of these figures when we concluded that "the only change produced by the antidote is an unimportant delay in the average time of death, due, we think, to the nature of the antidote, which delays absorption, rather than to chemical neutralization of the arsenious trioxide." We have never believed that there was a complete destruction of the toxicity of the arsenic. Dr. Wood seems also to infer that the prevention of vomiting in our experiment was an error. However, Bunsen and Berthold, in introducing this as an antidote, also prevented vomiting in their experimental animals. This they did by the rather objectionable method of ligating the oesophagus.

Now it seems perfectly legitimate to use a similar method in studying the effects of this alleged antidote at this stage as when it was introduced. Such a method, however, would never be used in the treatment, as is perfectly obvious. Our study, however, was not one of treatment but to test the value of the antidote.

Dr. Wood also thinks that we should have included the work of other investigators, especially those of Dr. Watt (*Ohio Medical and Surgical Journal*, 1861, page 287). Dr. Wood does not quote this article quite correctly when he says four animals received no antidote, all of whom died. The facts are seven received no antidote, of whom two recovered. We think it is of interest to give a synopsis of Dr. Watt's experiments as follows:

No. of expt.	Wt. of dog, lbs.	Amount As_2O_3 in grains.	Antidote.	Result.
1	50	2	None	Recovered 5 hrs.
2	60	3	None	Recovered 2 days
3	18	3	None	Died 6 hrs.
4	15	3	None	Died 8 hrs.
5	12	6	None	Died $1^1/_2$ hrs.
6	25	6	None	Died 6 hrs.
7	30	6	None	Died 5 hrs.
8	10	2	Antidote	Better 3 hrs.
9	15	3	Antidote	Better $1^1/_2$ hrs.
10	12	3	Antidote	Better 3 hrs.
11	35	4	Antidote	Recovered perfectly in 3 hrs.
12	20	4	Antidote	Recovered and partook of food in 3 hrs.
13	40	5	Antidote	Recovered in 8 hrs.
14	18	6	Antidote	Recovered in 8–9 hrs.
15	15	6	Antidote	Died 6 hrs.
16	25	6	Antidote	Gradually recovered
17	15	6	Antidote	Vomited a few times and showed no further signs of distress
18	18	6	Antidote	Showed no further signs of distress and no symptoms
19	15	7	Antidote	Soon recovered
20	25	7	Antidote	Recovered 5 hrs.
21	20	8	Antidote	Recovered in about 8 hrs.
22	30	8	Antidote	Recovered

Now it is perfectly obvious to anyone familiar with arsenical poisoning that recovery does not take place in a few hours as these experiments show. For this reason all such work has been ignored by pharmacologists. No one can say whether or not all of these animals would not have died inside two weeks, at any rate at a later date. If such had happened, as in the case of our own, we should consider that the antidote caused, at most, an unimportant delay in the time of death. This delay need not be due to any specificity, but to the volume of the antidote. Similar

results might have been obtained by using milk of magnesia, mucilage of acacia or anything that would have given volume. It is not necessary to run a series of experiments to prove this last statement, since it is a well-known and accepted fact in pharmacology that substances in the stomach delay the absorption and the action of poisons.

It is a notable fact in Watt's experiments that all his dogs vomited. This is the saving principle in all methods of treatment, and in this particular case, vomiting or removal of the poison is much more important than the chemical nature of the antidote. The volume, of course, aids in the elimination. In this respect we think that the action of ferric hydroxide with magnesium oxide U. S. P. does not differ from other voluminous inert matter.

HUGH MCGUIGAN, M.D.

HOTEL FACILITIES AT ASHEVILLE DURING A. PH. A. CONVENTION.*

It has been announced in this JOURNAL before that the American Pharmaceutical Association would meet in Asheville, North Carolina, on September 3–8 and that the Kenilworth Inn will be official headquarters.

It is not necessary that all attending delegates stop at the same hotel; they may distribute themselves to such other hotels than the Kenilworth as their choice dictates. There is given below a list of the houses in Asheville which are within convenient reach of official headquarters together with the rates they offer. The prices in every case are for each person. It is to be observed that most of the Asheville hotels are conducted on the American plan, as is the case in resort towns. Reservations should be made at once by delegates certain of attending the convention and as soon as possible by those who are now undecided.

GROVE PARK INN.

(American.)

All rooms with bath.

Two persons in room, each person	$9.00
One person in room	12.00

(As many as possible, but Insurance convention is meeting there, and they come first.)

BATTERY PARK.

(American.)

Single room without bath, each person	$6.00
Single room with bath, each person	8.00
Double room without bath, each person	5.00
Double room, with bath, each person	7.00

(Guests taking lunch away from hotel will be allowed $1.00 and for dinner $1.50.) (Can take 200.)

SWANNANOA-BERKELEY.

(European.)

Dble. room without bath, ea. person	$1.50–2.00
Dble. room with bath, ea. person	2.00–2.50

(Can take 40 to 50 "if they will double," but could not give single rooms.)

LANGREN.

(European.)

Single room without bath	$2.00–2.50
Double room without bath	3.00–3.50
Single room with bath	2.50–3.50
Double room with bath	4.50–6.00

(Can furnish 50 rooms.)

OFFICIAL HEADQUARTERS—KENILWORTH

(American.)

Single room without bath, each person	$8.00
Double room without bath, each person	7.00
Double room, with twin beds and private bath, each person	10.00–12.00
Double room with twin beds and use of connecting bath, each person	8.00
Fourth floor double rooms, twin beds, running water, each person	6.00

(Take 250.)

Other desirable hotels in Asheville are the Manor, with accommodations for 250, and Margo Terrace, with accommodations for 125. Both are on the American plan and both offer desirable quarters. However, neither promise convention rates to A. Ph. A. delegates.—J. G. BEARD.

*For rates and routes see under Societies and Colleges, in this issue of the JOURNAL.

EDITORIAL

E. G. EBERLE, Editor 253 Bourse Bldg., PHILADELPHIA

THE MODERN PHARMACY LAW, FINAL ACTION AT THE AMERICAN PHARMACEUTICAL ASSOCIATION MEETING IN SEPTEMBER.

THE Committee entrusted with drafting a Model for a Modern Pharmacy Law made its report and submitted its draft at the New Orleans Convention of the American Pharmaceutical Association. Its publication last year, owing to some minor changes decided upon by the Committee, came too late to permit final action by the Association at the Cleveland meeting, and it was then agreed that such final action should be taken at the Asheville meeting in September of 1923.

The Model submitted contains many new features and in some respects far-reaching changes. In the opinion of the Committee final action ought not to be taken until all who desire to be heard have had such opportunity. It will not be possible at any annual meeting to take the time for separately discussing every feature and section of the proposed Model. Most of the features and separate sections are certain to be unobjectionable and to receive unanimous approval, but there are a few regarding which there may be substantial differences of opinion. It has been the thought of the Committee that, in taking final action at the September Convention of the A. Ph. A., only those features and sections should be taken up separately regarding which there is a well-defined difference of opinion. To that end it was suggested that every one interested should study the draft with a view of picking out such features and sections as in their opinion required changes and be prepared to submit and advocate such changes when the draft of the law comes up for final consideration. It was suggested also that proposed changes, or such as were deemed desirable, might be submitted to the Chairman of the Committee, prior to the meeting.

Notice is now given for the last time that final action on the proposed draft of a Model for a Modern Pharmacy Law will be taken at the Asheville A. Ph. A. Convention during the week of September 3, 1923, and request is made for the last time that all who have changes to suggest, or to propose, send them either to the Chairman of the Committee, No. 1005 Mercantile Library Building, Cincinnati, Ohio, or be ready to submit them with reference to any particular section at the meeting. The final report of the Committee, including a complete draft of the proposed law, appears in the July 1922 number of the JOURNAL OF THE A. PH. A., pp. 566–575. Anyone interested, who may not have that issue of the JOURNAL, can secure a copy by addressing THE JOURNAL OF THE A. PH. A., 253 Bourse Building, Philadelphia.

FRANK H. FREERICKS,
Chairman Committee on Model for Modern Pharmacy Law.

BRINGING ABOUT A BETTER UNDERSTANDING OF PHARMACY BY THE PUBLIC.

WHILE full credit should be given to those who labored incessantly in New York for restricting ownership of drug stores to druggists—the Committees, the State Pharmaceutical Association, the New York Pharmaceutical Conference, etc.—it is indicative that citizens and their representatives are coming to a realization that protection is afforded the people when only those qualified by education and training, and who have a full appreciation of the responsibilities assumed by pharmacists, are permitted to engage in pharmacy, own and conduct drug stores.

The fact that many engaged in the drug business because of the opportunity afforded to profit by the sale of alcoholics was a powerful factor in making the passage of the law possible. It is probable that the necessity for the argument implied in the foregoing will, hereafter, not be as essential, because the people are coming to a better understanding of the protection given them by the service of qualified pharmacists—a point emphasized in bringing about the legislation referred to. Incidentally, this is a purpose of this comment, the drug exhibits during State association meetings, and at other times, have been helpful; this is good propaganda in which there should be close coöperation of the schools of pharmacy, pharmacists, and the associations.

Dr. Arthur T. McCormick, President of the Conference of State and Provincial Health Authorities of North America, recently said in an address:

"The medical colleges, medical societies, the hospitals and clinics are to be asked to join in bringing the profession closer to the people. It is proposed to have the health agencies in every country so organized and financed that medical knowledge will be available to all. In a way it is proposed to parallel what the Federal Government has done for agriculture by placing in every county a man who can bring direct to the farmers the essential facts of agricultural science. What the doctor now tells in technical language, if he tells it at all, is to be made available in every-day English for any man or any woman interested."

In such a coöperative endeavor pharmacists should join to bring the public to a better understanding of what pharmacy is and of the protection given them by right service—thereby misunderstanding will give way to a higher appreciation of the service of pharmacy and of pharmacists.

E. G. E.

SUMMARY OF ROCKEFELLER FOUNDATION ACTIVITIES.

WHILE pharmacy has not been a direct beneficiary by the gifts of the Rockefeller Foundation, there are pharmacists in the service of the institutions and promotions that have been given aid and become established during the first decennium of the organization. The work accomplished is of such large proportions that it has a general interest. President George E. Vincent has written a review of the

work and the volume will be issued shortly. Parts have been made public—the work done by the Foundation in 1922, directly and through its departmental agencies, the International Health Board, the China Medical Board and the Division of Medical Education, is summarized as follows:

Endowed chairs of medicine and of surgery in Hongkong University.

Pledged $1,125,000 toward new buildings for the College of Medicine of the State University of Iowa.

Contributed to the current maintenance of two medical schools in Canada.

Completed the buildings, strengthened the faculty and wholly financed the Peking Union Medical College.

Agreed to appropriate $300,000 toward laboratories and premedical teaching in two Chinese institutions, and in one missionary university in Peking.

Helped nineteen hospitals in China to increase their efficiency in the care of patients and in the further training of doctors and nurses.

Promised to coöperate in the rebuilding and reorganization of the medical school of Sao Paulo, Brazil, and of the medical school of Siam in Bangkok.

Made a survey of medical schools in Austria, Czechoslovakia, Germany, Hungary, Poland and Switzerland, and studies of English and Scotch methods of clinical teaching.

Sent eminent medical men as visiting professors or consulting officers to China, the Philippines, Brazil and Salvador.

Arranged for a commission of medical scientists from Strasbourg to visit the United States and England.

Gave emergency aid in the form of medical literature, laboratory supplies and apparatus, fellowships and stipends to promising investigators and teachers in the Pasteur Institute of Paris and in many other European centers.

Pledged $2,000,000 toward the site, building and equipment of a school of hygiene in London.

Coöperated with State boards of health in maintaining institutes and instruction for health workers.

Shared in malaria control in thirty-four country-wide and thirty-two town demonstrations in ten southern States and continued field studies and surveys in the United States, Porto Rico, Nicaragua, Brazil, Palestine, Australia and the Philippines.

Coöperated with the Mexican and other governments in steadily restricting the prevalence of yellow fever.

Resurveyed centers of hookworm infection in four southern States, and carried on control work in twenty-one foreign governmental areas.

Took part in promoting full-time health service in 163 counties in eighteen States of the United States, and in several counties in Brazil.

Agreeing to support for five years the disease-reporting service and for three years the international exchange of health personnel program of the health section of the League of Nations.

Provided fellowships in public health, medicine, nursing, chemistry and physics to 237 advanced students from twenty-three countries.

By consultation and providing of personnel aided public health administration in the United States, Australia, Brazil, Canada, Central America, Czechoslovakia, France, the Philippines.

Contributed to mental hygiene projects, demonstrations in dispensary administration, hospital information service surveys of nursing education and hospital management, the organization of tuberculosis work in France, the training of French health visitors, and other undertakings in the fields of public health and medical education.

There is an interdependence of the professions in the work promoted and made possible by the Foundation, and interrelation in scientific investigation to which Pharmacy has unselfishly and largely contributed.

E. G. E.

A MORPHOLOGICAL AND CHEMICAL STUDY OF NICANDRA PHYSALODES (L.) PERS.*,[1]

BY ANTON HOGSTAD, JR.

[Part of a thesis presented to the Faculty of South Dakota State College of Agriculture and Mechanic Arts, in partial fulfillment for the degree of Master in Science. June 1922.]

Botanical Studies.

INTRODUCTION.

Among the various plants that have been placed under cultivation in the Medicinal and Poisonous Plant Investigations Gardens of the South Dakota State College of Agriculture and Mechanic Arts School of Pharmacy, has been that of *Nicandra Physalodes* (L.) Pers., commonly known as the Apple of Peru. This plant has been placed under cultivation in the gardens since 1918, seed having been received from Professor E. L. Newcomb, in the fall of 1917. He reports that the seed had been purchased from Haage and Schmidt, Erfurt, Germany, in 1914.

The writer has undertaken a morphological and chemical study of the plant in question, on account of his interest in the *Solanaceæ*, especially in regard to the peculiar group of alkaloids that are present in a number of plants in this family.

Synonomy: *Nicandra*, Adans. (Calydermos); *Physalodes*, Boehm; *Nicandra Physalodes*, (L) Pers.; *Atropa Physalodes*, (L); *Atropa peruvianum*, Kuntze; *Physalodes physalodes*, Britton; *Nicandra physaloides*, (L) Gärt.

Common Names: Apple of Peru. Known as Belladonna de Pais in Mexico.

HISTORICAL.

The Apple of Peru is an old-fashioned garden herb, now rarely seen, adventive from Peru and sparingly naturalized in the United States. It is to be found at the present time in old gardens and waste places, being cultivated for its large, pale blue, showy flowers. Reported to be widely distributed in the tropics.

The plant is named in honor of Nicander† by Adanson, the specific name, *Physalodes*, being given by Boehmer, a German botanist.

It has been reported in literature to possess diuretic and narcotic properties. Pammel states that it is a poisonous plant and is used in some parts of the United States as a fly poison. Dujardin-Beaumetz, in their "Plantes Medicinales," states that a decoction of the plant is used in some of the tropical countries. The fruit is said to possess diuretic properties.

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* Scientific Section, A. Ph. A., Cleveland meeting, 1922.

[1] Acknowledgment.—The author wishes to take this opportunity of expressing his thanks to Prof. E. J. Petry and to Prof. E. R. Serles for aid in the preparation of this paper.

† Nicander (L. fr. Gr. Νικανδρος, Nikandros) was a Greek physician and hereditary priest of Apollo in his native city. Nicander was born in Claros near Colophon, in Ionia, 150 B. C. He was also a grammarian and a poet. Among his numerous works in verse and prose, two poems are extant. The first deals with remedies which were used for wounds inflicted by venomous animals, and the second on poisons and the treatment of poisons. Nicander was especially noted for his great work along toxicological lines, having been frequently quoted by Pliny, Galen and other ancient writers.

DESCRIPTION OF PLANT.

The Apple of Peru is a coarse, tall-spreading annual, which attains a height from 3 to 8 feet. The stem is distinctly ribbed and hollow; glabrous. The leaves are alternate, ovate or elliptic, blunt-pointed, from 2 to 12 inches in length and from 1 to 8 inches in width. Numerous multicellular non-glandular hairs are present

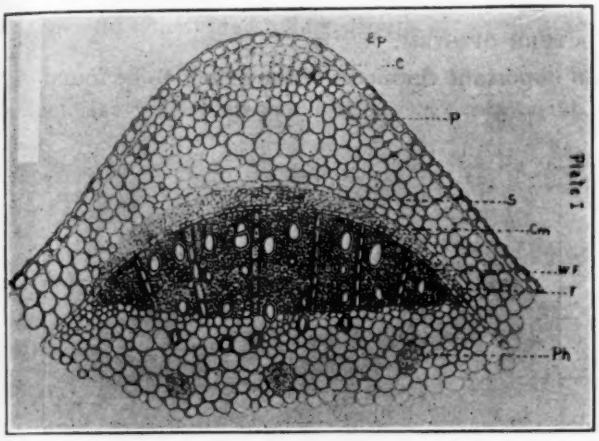


Plate I.—Transverse section through rib of young stem: Ep, epidermis; C, collenchyma; P, parenchyma; S, sieve; Cm, cambium; M, medullary rays; WF, wood fibers; T, tracheae; Ph, intraxylary soft bast; Pi, pith.

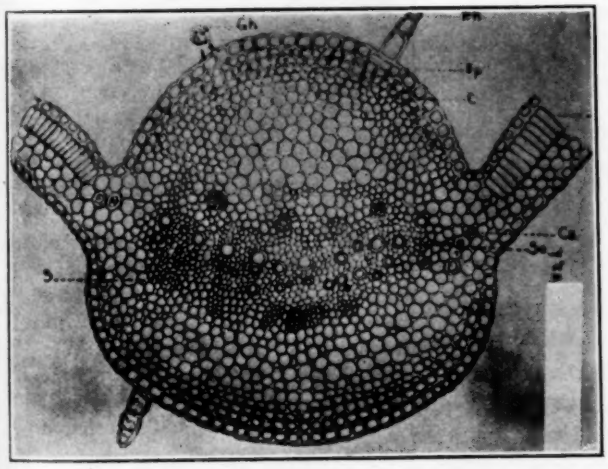


Plate II.—Transverse section, petiole: Ep, epidermis; Gh, glandular hair; Nh, non-glandular hair; C, collenchyma; T, tracheae; S, sieve; Ca, calcium oxalate; P, parenchyma; Pa, palisade tissue; Sc, sclerenchyma tissue.

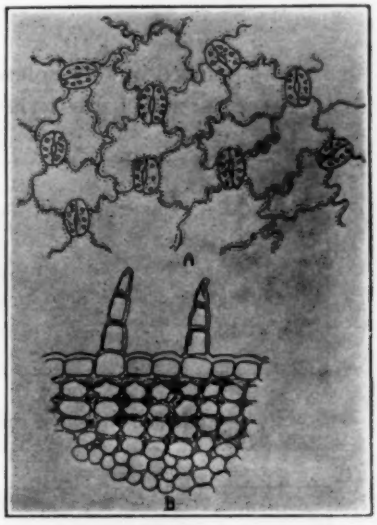


Plate III.—A, epidermal cells of leaf, showing stomata; B, transverse section petiole, showing epidermis, collenchyma and non-glandular hairs.

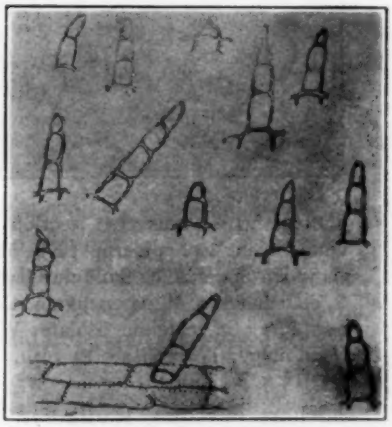


Plate IV.—Various types of non-glandular hairs.

on upper surface and along the margin of the leaf. The plant is grown for its large blue showy flowers, which are broadly campanulate, about an inch in length. Stamens 5, inserted on the corolla; anthers oblong; stigma 3- to 5-parted. Calyx

5-parted and which is much inflated in the fruit, loosely surrounding the latter. The fruit is a dry or nearly dry globular berry, about one-half inch in diameter. The fruit wall is thin and membranous, enclosing numerous small, brown seeds; 3- to 5-loculed, which differentiates the Apple of Peru from that of Physalis, the latter possessing a 2-loculed fruit. The Apple of Peru resembles that of a large Physalis and is often mistaken for the ground cherry and the winter cherry.

STRUCTURE OF STEM.

As pointed out by Solereder, an important character of the axis is to be found in the presence of intraxylary soft bast, which has been demonstrated by various

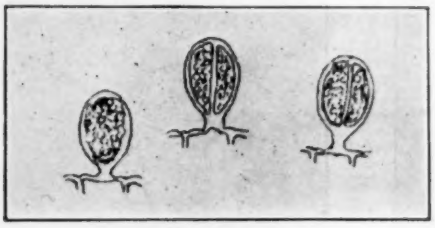


Plate V.—Various types of glandular hairs.

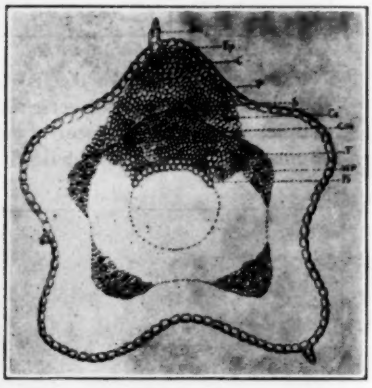


Plate VI.—Transverse section of young stem: Ep, epidermis; Nh, non-glandular hairs; Gh, glandular hairs; C, collenchyma; P, parenchyma; Cm, cambium; Ca, calcium oxalate; WF, wood fibers; T, tracheae; Pi, pith.

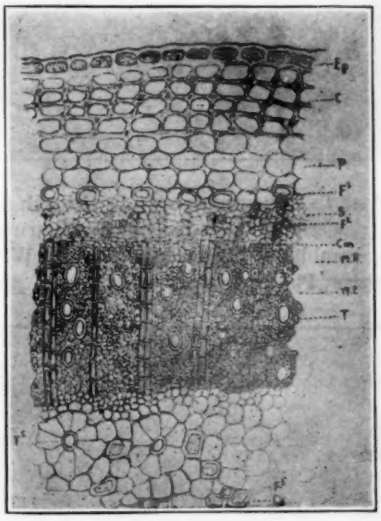


Plate VII.—Transverse section of mature stem: Ep, epidermis; C, collenchyma; P, parenchyma; F^1, bast fibers; F^2, bast fibers; S, sieve; Cm, cambium; Mr, medullary rays; WF, wood fibers; T, tracheae: T^1, tracheae (surrounded with stellate parenchyma); F^3, sclerenchyma fibers; Ca, calcium oxalate.

authors (Vesque, Radlkofer, Solereder, Schepegrell, Fedde) and which has been verified by the writer.

Sections of the mature stem present the following characteristics: a layer of uniform epidermal cells, with heavily thickened, cutinized outer walls and with thin radial walls; 3 to 6 layers of collenchyma, with distinct thickenings at the corners; cortex of parenchyma, in which are noted irregular-shaped crystals (prisms) of calcium oxalate, occurring singly or in the form of crystal fibers, associated

with the bast fibers; scattered elongated bast fibers; sieve area of characteristic form, among which is scattered a different type of bast fiber, the latter much shorter than those scattered throughout the cortical area; cambium, not clearly defined; xylem, consisting of heavily lignified wood fibers with thickened walls, tracheae of the simple and bordered pore type; medullary rays, 1 to 2 cells in width; pith composed of parenchyma cells, tracheae of single and double spiral type, around which are stellate groups of parenchyma cells; scattered sclerenchymatous

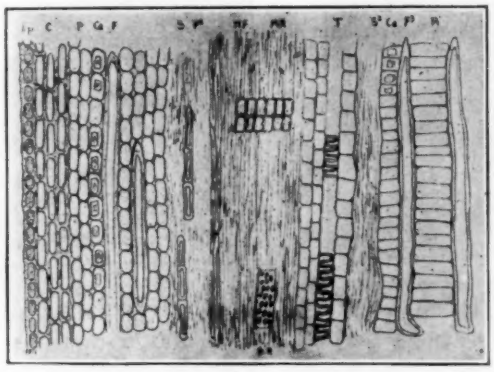


Plate VIII.—Longitudinal section of mature stem: Ep, epidermis; C, collenchyma; P, parenchyma; F, bast fibers; Ca, calcium oxalate; S, sieve; F^2, bast fibers; Cm, cambium; WF, wood fibers; T, tracheae; MR, medullary rays; S^2, intraxylary soft bast; F^3, sclerenchyma fibers; Pi, pith; BP, bordered pore tracheae.

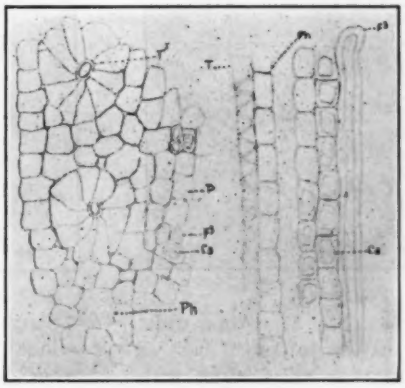


Plate IX.—A, transverse section of pith (mature stem); B, longitudinal section (same); T, tracheae; T^1, tracheae with stellate parenchyma; F^3, sclerenchyma fibers; Ph, intraxylary soft bast; Ca, calcium oxalate; P, parenchyma.

fibers, of the type found in the cortical region, and with which are associated crystal fibers; scattered patches of sieve (intraxylary soft bast—Solereder); central portion of stem hollow.

CHIEF STRUCTURAL CHARACTERISTICS OF LEAF.

Leaf bifacial; numerous multicellular non-glandular hairs on upper surface and along margin of leaf; the hairs being 2-4-5-celled in addition to the 3-celled hair as reported by Solereder; few small multicellular non-glandular hairs on both the upper and lower surfaces; stomata of usual shape, generally being surrounded by four neighboring cells; fibrovascular tissue of bicollateral type; irregular-shaped prisms of calcium oxalate in the parenchyma cells.

DESCRIPTION OF POWDER (LEAF MATERIAL).

Dark green; consisting of numerous large multicellular non-glandular hairs, which are from 2- to 5-celled, conical; a fewer number of smaller conical multicellular, non-glandular hairs; glandular hairs, club-shaped with short stalks, consisting of 1 to 2 cells, with vertical walls; calcium oxalate in the form of individual crystals and also in crystal fibers, the individual crystals in the form of irregular-shaped

prisms; stomata with fragments of accompanying epidermal cells; fragments of sclerenchymatous tissue; spiral and close annular tracheae; fragments or groups of cells filled with chlorophyll grains.

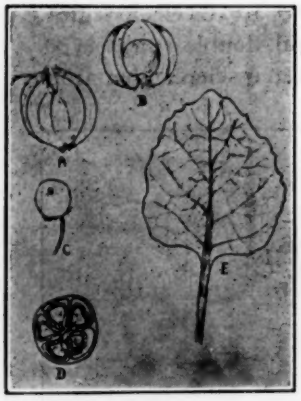
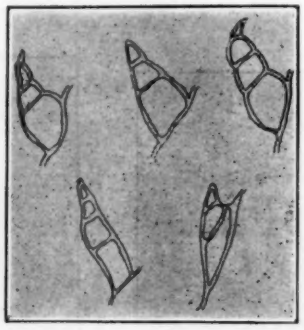


Plate X.—A, mature fruit; B, mature fruit with part of calyx removed; C, fruit with calyx removed; D, transverse section of fruit; E, leaf, $^1/_2$ natural size.



Part XI.—Types of multicellular non-glandular hairs from leaf.

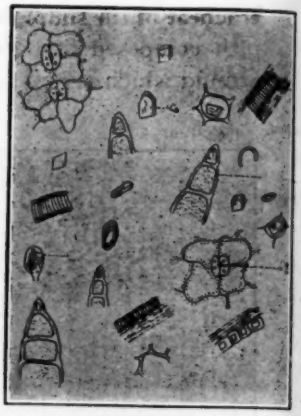


Plate XII.—Powdered leaf material; T, tracheae; Nh, non-glandular hairs; Ca, calcium oxalate; Cf, crystal fiber; Gh, glandular hairs; St, stomata.

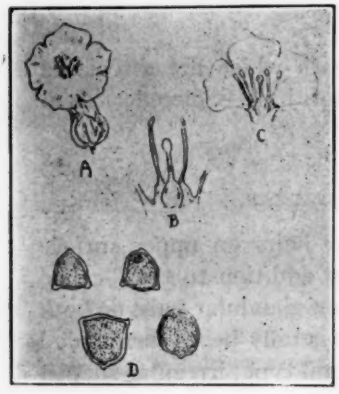


Plate XIII.—A, entire flower; B, C, longitudinal sections through flowers; D, pollen grains.

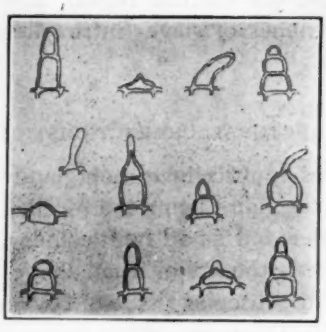


Plate XIV.—Types of multicellular, non-glandular hairs (from seedlings).

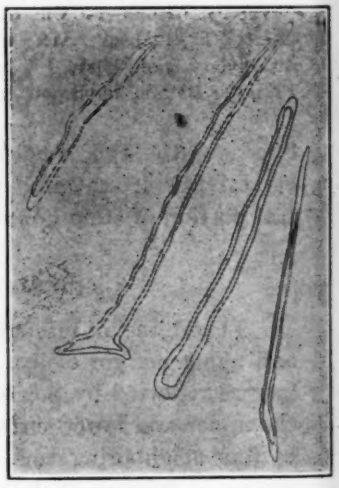


Plate XV.—Types of sclerenchymatous fibers from pith of mature stem.

CHEMICAL EXAMINATION.

The writer became interested in a study of *Nicandra Physalodes* (L) Pers., through the question of the alkaloids of the *Solanaceæ*. No reference has been noted in literature cited, in regard to the chemistry of this plant.

The present work only includes a preliminary investigation of the alkaloids of the Apple of Peru, the work to be continued, and reported upon at a later date, on the question of the Chemistry of the Alkaloids of *Nicandra Physalodes* (L.) Pers.

Qualitative tests for the presence of alkaloids were performed as follows:

1. Twenty-five grams of powdered leaf material were triturated with sufficient water during ten minutes and then filtered. Mayer's reagent was added to one portion and phosphomolybdic acid to another portion of the filtrate. No precipitate was produced in either case.

2. A like quantity of the material was triturated in a similar manner with sufficient dilute sulphuric acid (1/2 per cent.) and then filtered. A precipitate was produced in both cases with Mayer's reagent and with phosphomolybdic acid, apparently showing the presence of alkaloids.

Plate XVI.—Flat of seedlings, *Nicandra Physalodes* (L.) Pers., infected with *Pythium De Baryanum*.

3. Two hundred grams of powdered leaf material were extracted with 1/2 per cent. sulphuric acid, filtered, made alkaline with ammonia water and then extracted with chloroform. The chloroform extract was evaporated and recrystallized several times.

The finally purified alkaloidal material, when dissolved in 1/2 per cent. sulphuric acid solution, gave a distinct test for the presence of alkaloids with Mayer's reagent and also with phosphomolybdic acid, as well as a number of other alkaloidal precipitants in general use in the laboratory. The purified material was crystalline in nature and possessed the characteristic tobacco-like odor which is so generally noted in the assay of Solanaceous plants.

When assayed according to the method outlined in the United States Pharmacopœia, Ninth Decennial Revision, for Belladonnæ Folia, the leaves were found to contain 0.1 per cent. of total alkaloids. This has been verified by other workers in Drug Assaying Laboratory of the School of Pharmacy.

SUMMARY.

1. A morphological study of *Nicandra Physalodes* (L.) Pers. has been made and the following characteristics noted:

(*a*) Bicollateral type of fibrovascular tissue.

(*b*) Presence of 2-4-5-celled non-glandular hairs, in addition to the 3-celled type as reported by Solereder.

(*c*) The presence of an elongated type of sclerenchymatous fiber in the cortical and pith regions.

(*d*) The presence of calcium oxalate in the form of individual prisms of irregular shape and also in the form of crystal fibers.

(*e*) The presence of 1-2-celled non-glandular hairs with vertical walls.

2. Chemical study revealed the presence of alkaloids to the extent of 0.1 per cent. in the powdered leaf material.

Plate XVII.—Seedling, *Nicandra Physalodes* (L.). Pers.

Plate XVIII.—*Nicandra Physalodes* (L.) Pers. in Garden of Many Herbs, Medicinal and Poisonous Plant Investigations Gardens.

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2. Bentham and Hooker, "Genera Plantarum."
3. Britton and Brown, "Illustrated Flora of the Northern States and Canada."
4. De Bary, "Comparative Anatomy of the Phanerogams and Ferns," 1884.
5. Dispensatory, "The National, 3rd Ed."
6. Encyclopaedia, "The Britannica, 11th Ed.," 1910.
7. Encyclopaedia, "The New International, 2nd Ed.," 1915.
8. Engler und Prantl, "Die Natürlichen Pflanzenfamilien."
9. Gray, "New Manual of Botany."
10. Pammel, "Manual of Poisonous Plants."
11. Pharmacopœia, United States, IX.
12. Solereder, "Systematic Anatomy of the Dicotyledons."

ROCKEFELLER FOUNDATION DONATES £1,250,000 TO THE UNIVERSITY COLLEGE HOSPITAL AND LONDON UNIVERSITY GROUPS.

The cornerstones of the hospital buildings to be added to the University College Hospital and London University groups were laid May 31, a result of the £1,250,000 gift from the Rockefeller Foundation. This act evidences that the progress of science and the welfare of mankind is not limited by boundaries—the improvement of medical education and the advance of science to humanity—pharmacy should share in some of these gifts.

SOURCES OF MEDICINAL PLANTS AND SEEDS.

BY E. L. NEWCOMB.

The publication of the list of plants now growing in the different medicinal plant gardens throughout the United States by Dr. W. W. Stockberger of the U. S. Bureau of Plant Industry has apparently given an impetus to drug plant cultivation. The College of Pharmacy of the University of Minnesota has had numerous inquiries for medicinal plants and seeds. A word on the source of supplies seems, therefore, to be in order.

The nature of many of the inquiries indicates that some who are attempting to develop medicinal plant gardens have little conception of the seed, plant and nursery business of this country and Europe. Collectively this is a very large industry. A number of the firms began their activities about one hundred years ago. The chief aim of these firms is to supply seeds and plants for the production of vegetables and fruits or for the development of flowering and ornamental plants, shrubs and trees.

The writer was brought up in the seed and plant business and has kept more or less closely in touch with it for some thirty years. So far as is known none of the larger firms devote attention primarily to medicinal plant seeds or stock, but many give separate lists of the more common garden herbs. Some specialize along certain lines, as for example: evergreen stock, bulbs, small fruit stock, rose stock, native perennial plants of given localities, tropical plants, cactus, etc.

The history of drugs reveals the fact that practically every plant has at one time or another been used experimentally or otherwise in medicine. The collections of the florist, the seed dealer or the nurseryman, therefore, contain many of our more or less well known medicinal plants. As a matter of fact one of the largest seed and plant houses in the world lists practically everything in the recent compilation issued by Dr. Stockberger.

It should be borne in mind that the efforts of those engaged in the seed and plant business have not been directed toward the production of plants to be used for the preparation of drugs. Their aim has been to produce plants with the most beautiful flowers or the finest fruit, or the most nutritious and valuable vegetables and grain. They have, with the exception of the cereals and a few extensively grown fruits and vegetables, paid practically no attention to plant constituents.

Hybridization and selection has been extensively practiced by the seed and plant growers. Innumerable garden varieties have been produced. A few good botanical varieties have been discovered and a still lesser number of mutants representing good species. Trade names have been given galore to strains of varieties and species possessing but slight differences. It may be said that for the most part scientific botanical names have been eliminated by those who grow seed or plants for commercial purposes. It is no doubt quite impossible to determine the botanical origin of some of the garden varieties and hybrids now offered.

On the other hand some firms endeavor to supply true type botanical species in addition to the various strains and selections. As a rule seed and plant dealers supply material true to label. Occasionally errors are made. *Delphinium ajacis* continues to be sold for *Delphinium consolida*. Some offer the so-called *Valeriana rubra* for *Valeriana officinalis*, etc. Continued cultivation may cause slight va-

riation in the characteristics of the native plant. Conditions of soil, climate, etc., all have their effect. These, however, are some of the problems of the pharmacognocist which must be solved with the medicinal plant garden.

In the light of recent discoveries which show the importance of such substances as the vitamins, thyroxin and insulin in animal metabolism it becomes evident that our entire vegetable materia medica must be re-studied. The strains and garden varieties of medicinal plants may or may not yield the desired results. The fact that we have them does not mitigate against the development of the medicinal plant garden, it rather facilitates our work. We may find the desired qualities in some of these garden forms, or we may find that the type species is most valuable. Enough work has been done to show that plant breeding often has a direct relation to medicinal constituents. In other cases this appears not to be true. With the leaves of the different varieties of *Digitalis purpurea* we find about the same amount of therapeutic activity.

A source of supply in getting the medicinal plant garden started, which is often overlooked, is the drug itself. It is surprising what a large number of our whole vegetable drugs contain seed of the plants yielding the drug. A few seed will not retain their germiable qualities more than a year. The majority will germinate in fairly large percentage even after several years of storage. At the present time, June 1923, we have seed of the plants yielding Colocynth, Poppy Capsules, Belladonna, Capsicum, Lobelia and many other drugs, germinating and growing nicely, and all were separated from drug stock. We have grown a very large number of medicinal plants in this way. It is interesting to note that the botanical identity of plants produced in this manner is not always in accordance with official definitions. Varieties and strains which for the most part are not mentioned in our definitions are also to be met with. Some of these seed from the drug stock germinate slowly and one must not become impatient and discard the planting too soon.

Such products as mustard seed or the umbelliferous fruits may be obtained in the retail drug store. These if fairly fresh will usually grow. Recently we had the unique experience of spending the time and energy necessary to wrap up and ship halfway across the United States two ounces of flaxseed in order that one of our medicinal plant gardens might have growing the plant yielding this drug. We were glad to render the service but hope that the near future will see more enlightenment on sources of supply.

It is very fortunate that through the compilation by Dr. Stockberger directors of medicinal plant gardens are now able to coöperate more effectively with each other in exchanging plant material. This will be especially helpful in the exchange of plant material which is native of given localities. This school is always glad to coöperate along these lines.

Our sources of supply may then be summarized under the following general heads:

1. The seed, plant and nursery dealers.
2. The vegatable drug stock of the retail pharmacist, the wholesale druggist or the college of pharmacy collections.
3. The fields and woods where our native American drug plants may be collected.
4. The exchange between our different medicinal plant gardens.

The question of correct botanical identity is one which must be established in the garden or at the institution where the plants are grown, and this for the most part regardless of the source of the material.

The director of every medicinal plant garden in the country should have available the seed and plant catalogues of a representative list of firms. The following are merely suggested. There are many others, possibly some issuing equally extensive lists.

REPRESENTATIVE AMERICAN SEED AND PLANT DEALERS.

Henry A. Dreer, 714–716 Chestnut Street, Philadelphia, Pa.
Peter Henderson & Co., 35 and 37 Cortlandt St., New York.
D. M. Ferry & Co., Detroit, Michigan.
Northrup, King & Co., Minneapolis, Minn.
W. Atlee Burpee Co., Seed Growers, Philadelphia, Pa.
J. M. Thorburn & Co., 53 Barclay St., New York, N. Y.
The Storrs and Harrison Co., Painesville, Ohio.
Wm. Henry Maule, Inc., 21st and Arch Sts., Philadelphia, Pa.
Vaughn's Seed Store, 43 Barclay Street, New York, N. Y.
Otto Katzenstein & Co., Atlanta, Ga.
Hopedale Nurseries, Hopedale, Ill.
Royal Palm Nurseries, Reasoner Brothers, Oneco, Fla.
Fredk. H. Horsford, Charlotte, Vermont.
Carl Purdy, Ukiah, California.
Rose Hill Nursery, P. O. Box 495, Minneapolis, Minnesota.
Jewell Nursery Co., Lake City, Minnesota.
L. L. May & Co., Inc., St. Paul, Minnesota.
D. M. Andrews, Rockmont Nursery, Boulder, Colo.
The Bay State Nurseries, North Abington, Mass.

FOREIGN SEED AND PLANT DEALERS.

Haage & Schmidt, Erfurt, Germany.
Henry Mette, Quedlinburg, Germany.
Vilmorin-Andrieux & Cie, 4 Quai de la Magisserie, Paris, 1 r, France.
Sutton & Sons, The King's Seedsmen, Reading, England.
Kelway and Sons, The Royal Horticulturists, Langport, Somerset, Eng.
James Veitch & Sons, Ltd., Chelsea, England.
Felix & Dykhuis, Boskoop, Holland.
C. G. Van Tubergen, Jr., Haarlem, Holland (Zwanenburg Nurseries)
(E. J. Krug, New York Agent, 110 Broad St., Centennial Bldg.).
Yokohama Nursery Co., 21–35 Nakamura, Yokohama, Japan.
C. Starke & Co., Mowbray, Cape Province, South Africa.
Jardin Correvon, Geneva, Switzerland.

GREENHOUSES AND GREENHOUSE SUPPLIES.

Lord & Burnham Co., St. James Bldg., New York City.
Pierson U-Bar Co., Metropolitan Bldg., 1 Madison Ave., New York, N. Y.
John C. Moninger Co., Chicago, Ill.
E. H. Hunt, Greenhouse Supplies, 129 N. Wabash Ave., Chicago, Ill.
King Construction Co., North Tonawanda, N. Y.

The addresses furnished above are given simply as information, with the understanding that the list is not complete.

Experiments should be conducted in germinating all seed that may be separated from the drug stock. Some very fine results may be obtained from this source of supply. We have grown from seed separated from the drug stock the plants yielding many drugs. The following we have experimented with, those marked with an asterisk, successfully.

*Adonis
*Almonds—Bitter and Sweet
*Anise
*Anthemis
Areca
Arnica Flowers
*Belladonna
Black Hellebore
Buchu
*Buckthorn
*Cannabis, American and Indian
*Capsicum
Cardamom Seed
*Carum
*Cataria
*Cassia Fistula
*Celery
*Centuary
*Chenopodium
Chirata
Citrullus
Cocculus
Coffea (Unroasted)
Colchicum
*Colocynth
*Concium
*Coriandrum
Croton
Cubeba
Damiana
*Delphinium
Euphorbia
Foenugreek
*Foeniculum
*Galega
Green Coffee
*Grindelia
Helianthemum
*Hyoscyamus
Ignatia
*Juniperus
*Lappa (Seed)
Laurel Berries
*Linum
*Lobelia
*Malva Leaves and Fruit
*Melilotus
*Millefolia
Nux Vomica
*Pepo
Pepper—Black and White
*Petroselinum
Pimenta
*Phytolacca
Physostigma
*Poppy
*Prickly ash berries
Pyrethrum—open and closed
*Rhamnus Cathartica
*Rhus Glabra
Sabal
Santonica
*Senecio
Senna
Serphyllum
*Scoparius
*Scutellaria
*Siliqua
*Sinapis Nigra
*Sinapis Alba
Star anise
*Stavesacre
*Stramonium (Seed)
Strophanthus
*Tamarind
*Verbena

Finally, field trips in search of native medicinal plants are urged as a regular part of every pharmacy curriculum. Students profit greatly by such excursions. Instruction in the proper method of collecting, transplanting and conserving native medicinal plants give such trips increased value and interest to the student. Great care should always be exercised to see that plant material is not unnecessarily destroyed. Each college of pharmacy maintaining a medicinal plant garden should endeavor to specialize in a degree upon medicinal plants native of the locality. This policy, if followed out for a few years, will greatly improve our facilities for exchanging material and increase our knowledge of our native medicinal plants.

Department of Pharmacognosy,
College of Pharmacy,
University of Minnesota,
June 1, 1923.

PHYTOCHEMICAL NOTES.*

No. 93. Balsam of White Fir.[1]

BY. S. S. AIYAR.

A number of years ago a special study was made of the so-called Oregon balsam. Not only were the physical and chemical constants of this substitute[2] for Canada balsam determined in connection with commercial specimens, but an attempt was also made to ascertain its botanical source. For the latter purpose a number of balsams were secured and examined.[3] It was in this connection that the U. S. Forest Service had collected between July 24 and 30, near Camptonville, California, in the Tahoe National Forest[4] a small amount (about 8 ounces) of balsam from white fir, presumably *Abies concolor* (Gord.) Parry.[5] This material has at last been examined.

The balsam was almost colorless when it arrived and has remained thus after these many years. It is still semifluid though not quite as mobile as when fresh. In the course of years it has deposited a white flocculent precipitate. Its odor is still not unpleasantly terbinthinate.

The density, determined at 20° in a specific gravity flask, was 0.989. Its optical rotation in a 50 mm. tube was +5.53°. The angle of rotation of its 25 p. c. chloroformic solution was +4° 61′ in a 100 mm. tube. In alcohol it is soluble for the most part but leaves a white residue. This is likewise true of such solvents as acetone, and benzene in the cold. In the case of benzene, the residue is very small. In chloroform and ether the balsam is completely soluble. Distilled with steam, the oleoresin yielded 27.7 p. c. of oil, the resin remaining as a brittle amorphous mass when cool.

VOLATILE OIL.

The volatile oil was colorless and had a distinctly terebinthinate but pleasant odor. $d_{20°}$ 0.865; α_D + 11.88°.

Upon direct distillation it yielded the following fractions:

t.	Amt., Gm.
–154°	1.4
154–156°	3.0
156–164°	16.9
164–166°	6.0
166–174°	1.9
174–176°	0.35
176°+	0.3
Total,	29.85

* From the laboratory of Edward Kremers.

[1] Scientific Section, A. Ph. A., Cleveland meeting, 1922.

[2] See "Phytochemical Notes No. 56," *Ph. Rev.*, 22, p. 293.

[3] "Phytochemical Notes," 59 (*Ibid.*, 23, p. 46) and 79 (JOUR. A. PH. A., 2, p. 1566).

[4] The label on the bottle recorded the dates given above, but not the year. The correspondence with U. S. Forest Service contains a letter with reference to red fir, but not to white fir, hence the year cannot be supplied.

[5] This is the botanical designation as given by Schorger in his article: "The Leaf and Twig, and Bark Oils of White Fir," *Jour. Ind. Eng. Chem.*, 6, p. 809.

As will be seen, the bulk of the oil came over between the pinene and no pinene fractions. Fraction 164–166° deviated the ray of polarized light +12.92°, hence its angle of rotation differed but little from that of the entire oil.

The presence of pinene in fraction 154–156° was readily demonstrated by converting it into the nitrosochloride and this into the nitrolamine base. However, the latter melted at 126–127°, whereas the melting point of pinene nitrolpiperidine is recorded at 118–119°. Possibly this difference is due to impurities in the reagent discovered later.

RESIN.

In order to obtain, if possible, a crystalline resin acid from the resin left after steam distillation of the oleoresin an attempt was made to dissolve the former in alcohol. However, in this solvent it is found to be but sparingly soluble. The hot alcoholic solution, upon cooling, deposited a granular white precipitate. More of it was soluble in acetone, which solution, upon evaporation of the solvent, deposited a transparent amorphous resin. Benzene dissolved it even more completely. In ether and chloroform the resin is readily soluble.

In order to effect at least a partial separation of the several constituents, the bulk of the small amount of resin available, was extracted with alcohol, the hot alcoholic solution filtered and the filtrate allowed to cool. Thus a very small amount of a white crystalline powder was deposited, too small indeed for further investigation.

The alcohol insoluble resin was then extracted with acetone. The acetone extracted a large portion of the resin, but would not crystallize it out. Hence the solution was concentrated by evaporation and allowed to cool, when the whole mass cooled down to a thick syrupy liquid. As no crystals could be obtained, all the acetone was driven off and the resin obtained as a brown translucent mass easily pulverized.

The residue was again extracted with alcohol-benzene mixture. A small portion of the resin was soluble but would not crystallize even on concentrating the solution. When all the solvent was driven off a yellow plastic resin was left.

The residue was a white solid with a saponification value of 130.5 and 115.3. The reason for this difference in value of the duplicates is due to the fact that the resin melts to a globule, and does not expose a free surface to the reacting liquids.

The original resin itself had a saponification number of 120.9. The resin extracted by acetone gave a saponification number of 143.4. It seems as though the acetone takes up more of the acid material. Again another sample of original resin 30 Gm. in weight was extracted with 400 cc alcohol. On cooling the solution a small quantity of white precipitate was obtained.

CONTRIBUTIONS TO THE KNOWLEDGE OF FOREST PRODUCTS.

VI. On Hydrazino-2 Cymene and Some Other Compounds Derived from Amino-2 Cymene.[1]

BY W. A. DEMONBREUN AND R. E. KREMERS.

The amino-2 cymene prepared as previously described[2] was used in the following preparations.

Hydrazino-2 Cymene.—The diazotization of the base by hydrochloric acid and sodium nitrite and the subsequent reduction by stannous chloride were tried according to the usual method several times,[3] but without much success. The following procedure gave better results.[4]

Two hundred and fifteen cc of concentrated hydrochloric acid was added to 25 grams of amino-2 cymene in a deep porcelain beaker placed in a freezing mixture of salt and ice. An electrically driven stirrer was then started in the mixture, causing most of the hydrochloride to go into solution. When the temperature had fallen to —5° C., a solution of 15 grams ethyl nitrite in 15 cc of alcohol was added drop by drop from an ice-cooled burette. The temperature was kept below 0°. The diazotizing mixture passed through all the color changes just as in the diazotization of aniline.

After the nitrite solution had been added, a slight excess of nitrous acid was present. To the solution, still cooled and agitated, was added a solution of 150 grams stannous chloride in 125 cc of conc. hydrochloric acid, also cooled to 0°. The cymylhydrazine separated as a pinkish white precipitate which collected at the surface of the liquid on standing. It was filtered out by suction and when nearly dry was decomposed by the addition of an excess of strong caustic soda solution. When the decomposition was complete, the free base, which separated as a light red colored oil, was extracted with ether. This solution was dried over anhydrous sodium sulphate and the ether distilled off from the water-bath. The residual viscous oil was finally purified by vacuum distillation. The largest yield of crude hydrazine was 19 grams, or 69 per cent.

The data from a fractionation under 1.5 mm. pressure—considerable decomposition took place at 13 mm. pressure maintained by a water pump—are given as representative of our best results.

Fraction.	B. p. 1.5 mm.	Weight, Gm.	n_D
1	–95° C.	12	1.5083
2	95–110	2	1.5260
3	110–15	3	...
4	115–20	7	1.5502
5	120–30	4	1.5443
6	130+	3	...

Fraction 1 was almost colorless, insoluble in hydrochloric acid, and without action on Fehling's solution.

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[1] Based on part of a thesis submitted by W. A. D. to the Graduate Faculty of Vanderbilt University in partial fulfillment of requirements for the degree of M.S., June 1922.

[2] See Contribution V, Jour. A. Ph. A., p. 296, April issue, 1923.

[3] Cohen, "Practical Organic Chemistry."

[4] Compare with Weyl, "Die Methoden der Organischen Chemie," pp. 817, 819.

Fraction 2 was partially soluble in hydrochloric acid, and reduced Fehling's solution.

Fractions 3 and 4 were completely soluble in hydrochloric acid, reduced Fehling's solution, and had a light yellow color.

Fraction 5 was darker in color and smelled of ammonia. The residue was a red tar.

Considering fractions 3 and 4 as pure hydrazine, the yield is 21 per cent. of the aminocymene.

Hydrazino-2 Cymene Hydrochloride.—The hydrochloride was prepared by adding a slight excess of concentrated hydrochloric acid to the free base. The resulting solid was dissolved in 5 per cent. alcohol and reprecipitated by the addition of conc. acid. The white needle-like crystals were separated from the mother liquor by filtration, washed with water, and dried. M. p. 186–7° C.

Aqueous or alcoholic solutions of this compound decompose during evaporation, even under diminished pressure.

Nitrogen by Dumas method = 14.16 p. c.
Nitrogen in $C_{10}H_{16}N_2.HCl$ = 13.97 p. c.

Acetylhydrazino-2 Cymene.—The acetyl derivative was prepared by adding a slight excess of acetic anhydride to the free base. The resulting reaction was completed by warming the solution for a few minutes on a water-bath. The new compound was isolated by pouring the warm reaction mixture into cold water. The precipitated straw colored solid was recrystallized from 50 per cent. alcohol, and then from ether. There resulted almost white, scaly crystals, of m. p. 125–6°.

Nitrogen by Dumas method = 13.87 p. c.
Nitrogen in $C_{10}H_{13}.N_2H_2.C_2H_3O$ = 13.59 p. c.

Glucose Cymylhydrazone.—One mole of cymylhydrazine hydrochloride was dissolved in a 1 per cent. solution of glucose containing one mole of sugar. The solution was then made acid with acetic acid by the addition of a slight excess of anhydrous sodium acetate. On standing the hydrazone precipitated. The compound was filtered out by suction, recrystallized from 50 per cent. alcohol, and dried as quickly as possible.

The product was a yellow mass of fibrous crystals. M. p. 92–3° C.

Nitrogen found by the Dumas method = 8.87 p. c.
Nitrogen in $C_{16}H_{26}O_5N_2$ (hydrazone) = 8.59 p. c.
Nitrogen in $C_{26}H_{38}O_4N_4$ (osazone) = 11.91 p. c.

Mannose Cymylhydrazone.—The mannose compound was prepared in the same manner as the preceding substance. M. p. 110–11° C.

Nitrogen found by the Dumas method = 9.09 p. c.
Nitrogen in $C_{16}H_{26}O_5N_2$ = 8.59 p. c.

Galactose Cymylhydrazone.—This compound was prepared by the same method as its analogues. M. p. 149–50° C.

Nitrogen found by the Dumas method = 9.42 p. c.
Nitrogen in $C_{16}H_{26}O_5N_2$ = 8.59 p. c.

Glucose Osazone.—In experimenting with the action of hydrazino-2 cymene on glucose, the conditions first chosen were analogous to those obtaining in the preparation of glucose phenylosazone. That is, 3 moles of the hydrazine hydrochloride to one mole of glucose were dissolved in water, treated with sodium acetate, and the filtered solution heated gently on a water-bath. The resultant precipitate was always grossly contaminated with a tar that could not be removed by recrystallization. Furthermore the nitrogen content was always too low, and the compound when partially purified began to approximate the properties of the glucose hydrazone described above.

In view of these facts, it seems reasonable to conclude that hydrazino-2 cymene reacts readily but once with aldose sugars; that is, the reaction practically stops with the formation of hydrazones. This is in decided contrast to the behavior of phenylhydrazine, which forms osazones very easily in certain cases, and is analogous to the behavior of *o*-tolyl hydrazine. The uniformly rather high nitrogen content may raise a question as to just what has happened. But the values lie closer to the hydrazone than to the osazone. And in view of the ready decomposition of these substances, a variation from the theoretical values is not surprising.

Benzaldehyde Cymylhydrazone. Furfural Cymylhydrazone.—The preparation of hydrazones of benzaldehyde and furfural was attempted as one of the first reactions in the study of our hydrazine fractions. It was thought that these compounds would be readily crystallizable and that they would aid in their characterization. While reactions undoubtedly took place, only red-colored tars resulted that defied crystallization.

Acetoacetic Ester Derivative.—Various fractions and preparations of hydrazino-2 cymene were involved in reaction with acetoacetic ester. It was thought that pyrazolone formation might result as in the case of phenylhydrazine. There can be no doubt that these two substances react because heat is evolved and drops of water separate when they are brought together. However it was not possible to effect the formation of a crystalline substance. The amount of material at our disposal was too small for purification by distillation *in vacuo*, hence no analysis was made. It is therefore impossible to decide whether a ketone ester hydrazone resulted, or a liquid pyrazoline. We are inclined to the supposition that the former is the case because of the behavior of hydrazino-2 cymene toward the aldohexoses

$$CH_3.CO.CH_2.CO_2.C_2H_5 + H_2N{-}NH{-}C_{10}H_{13}$$

1. Ketone-ester hydrazone

$$CH_3{-}C(=N{-}NH{-}C_{10}H_{13}){-}CH_2{-}CO_2{-}C_2H_5 + H_2O.$$

2. Pyrazolone derivative

$$CH_3{-}C(=N{-}){-}CH_2{-}CO{-} + C_2H_5OH.$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad -N{-}C_{10}H_{13}$$

In addition to preparing hydrazine-2 cymene from amino-2 cymene, preliminary experiments were made with two other compounds.

Cymyl Urea.—Cymyl urea results when amino-2 cymene hydrochloride and potassium cyanate are allowed to react in the usual way. After recrystallization from hot alcohol, diluted with water, the compound forms white, needle-like crystals. M. p. 162–3° C.

$$C_{10}H_{13}{-}NH{-}CO{-}NH_2.$$

Sym. Cymyl Phenyl Urea.—Phenylisocyanate and amino-2 cymene react vigorously on being brought together. The product recrystallized from 5 per cent. alcohol forms light, fluffy, white crystals of m. p. 192° C.

$$C_{10}H_{13}—NH—CO—NH—C_6H_5.$$

SUMMARY.

1. Hydrazino-2 cymene (synonyms; cymyl hydrazine, carvacryl hydrazine) has been prepared from amino-2 cymene, together with its hydrochloride; monoacetyl derivative; glucose, mannose, and galactose hydrazones.

2. The cymyl hydrazones of benzaldehyde and furfural were not obtained in crystalline form.

3. Cymyl hydrazine reacts readily with acetoacetic ester, but the exact nature of the product has not been determined.

4. There is evidence that the side chains of the cymene residue exert a steric hindrance in some reactions of hydrazino-2 cymene.

5. Cymyl and sym. cymyl phenyl urea have been prepared.

SYNTHETIC DRUGS—IV.*

EXAMINATION OF AMERICAN-MADE CHLORAMINE-T, DICHLORAMINE-T, HALAZONE AND PREPARATIONS.

BY PAUL NICHOLAS LEECH, PH.D., CHICAGO.

Six years ago Dakin, Cohen and Kenyon[1] introduced into medicine the first "chloramine" antiseptic, "Chloramine-T;" the other members of the family, "Dichloramin-T" and "Halazone," followed soon afterward. The history of their introduction and of their commercial preparation has been detailed repeatedly in the pharmaceutical and medical literature; discussion now would be repetition.

The Council on Pharmacy and Chemistry of the American Medical Association kept pace with the therapeutic progress attendant on war times and described these chlorine antiseptics in "New and Nonofficial Remedies" after standards had been drawn up by the A. M. A. Chemical Laboratory. Since then a number of American firms have been marketing the products. It seemed opportune at this time to determine the purity of the market supply of those products described in "New and Nonofficial Remedies" and particularly to investigate the stability of the compounds containing a somewhat unstable atom. Hence this present report.

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* Contribution from the Chemical Laboratory of the American Medical Association.

The previous articles were: "Examination of American-Made Acetylsalicylic Acid," *J. Ind. and Eng. Chem.*, April, 1918, p. 228 (see also editorial, *Ibid.*, April 1918, p. 225); "American-Made Synthetic Drugs—II. Examination of Procaine (Novocain), Barbital (Veronal), Phenetidyl-acetphenetidin (Holocain), Cinchopen (Atophan), Manufactured under Federal Trade Licenses" (with Wm. Rabak and A. H. Clark), *J. A. M. A.*, 73, 754 (Sept. 6), 1919; "Synthetic Drugs—III. The Digestion of Tannin Compounds Used as Intestinal Astringents by Artificial Digestive Mixtures," *J. A. M. A.*, 75, 1120 (Oct. 23), 1920.

[1] *British Medical Journal*, Jan. 29, 1916, p. 160.

COMPARISON OF CHLORAMINES AND "SURGICAL SOLUTION OF CHLORINATED SODA."

The chloramines and their predecessor "Surgical Solution of Chlorinated Soda" ("Dakin's Solution") have one point in common which seemingly has been overlooked in the many comments on this topic. Both possess the positively charged and relatively unstable chlorine atom (Cl^+) and hence are active oxidizing agents in the proper medium.[1] Many writers have stressed the point that the Surgical Solution of Chlorinated Soda differs from the chloramines because it liberates oxygen and is, therefore, an oxidizing agent. This explanation is a relic of past days when sodium hypochlorite or hypochlorous acid was presumed to act as $2HClO \longrightarrow 2HCl + O_2$.

In the light of modern chemistry, however, we no longer hold the view that oxygen, directly or indirectly, is necessary for oxidation. Instead oxidation may "be considered to involve ultimately the assumption of positive or the loss of negative electrical charges by ions or atoms" and defined "as consisting fundamentally in the *loss of electrons by atoms or ions.*"[2] Thus hypochlorous acid [(ClOH) which besides ionizing to H^+ and ClO^-, dissociates to Cl^+ and OH^-]; hypobromous acid (Br^+OH^-) and their derivatives have a common characteristic, an atom with an unstable positive charge and a tendency to convert this atom to the common stable negative variety[3] (as for instance Chloride (Cl^-)).

There is convincing evidence to show that chloramine antiseptics contain positively charged chlorine: (1) The formulas and the methods of preparation (the replacing of a hydrogen atom of an amid group by chlorine) strongly suggest that the chlorine is positively charged. (2) On hydrolysis, they yield hypochlorous acid. (3) They are active oxidizing agents.

Thus the chloramines may be considered as simply more adaptable forms of administering the positive chlorine, which is well known medically in the form of sodium hypochlorite (Cl^+ONa), or bleaching powder. The antiseptic action of these is most probably due to the oxidizing action of a positively charged chlorine, in the case of the hypochlorite, the chlorine atom is bound to a hydroxyl group; in the case of the chloramine, to a nitrogen ($N\equiv$) atom.[4]

OXIDIZING ACTION OF CHLORAMINE-T.

Accepting the premise that Chloramine-T is an antiseptic by oxidation because it contains the relatively unstable chlorine atom (Cl^+), which tends to go over to the stable form (Cl^-), the question arises what effect will the reaction of the solvent have on the oxidation potential. Is it more active in acid; neutral or alkaline solution? In elaborating Chloramine-T standards for the Council on Pharmacy and Chemistry, one of the first reactions noted was that when a

[1] The two main attributes of the Surgical Solution of Chlorinated Soda are: (1) a definite degree of alkalinity sufficient to be of value in removing necrotic tissue but not too great to be unduly irritating; the p_H should be between 8 and 10; (2) the solution should be hypertonic. For methods of preparing such a solution see "New and Nonofficial Remedies," 1922, p. 137.

[2] Julius Stieglitz, "Quantitative Chemical Analysis," The Century Company, 1911, Part I, p. 252.

[3] Stieglitz and Senior, *J. Am. Chem. Soc.*, 38, 2727, 1916.

[4] Those interested in the electronic aspect of the nitrogen valences are referred to Stieglitz and Leech, *J. Am. Chem. Soc.*, Feb. 1914, 36, p. 272, and to references therein, also Stieglitz, *Ibid.*, June 1922, 44, p. 1293.

dilute solution of Chloramine-T was added to potassium iodide solution, iodine was freed, but in the case of potassium bromide solution, no bromine was freed; yet, when the latter solution was acidified, bromine was freed. In fact, this test can be used advantageously for a simple qualitative distinction between bromides and iodides. This shows that the oxidating action is increased in acid solution, and that, in common with ferric chloride, Chloramine-T in neutral solution has sufficient oxidizing action to oxidize an iodide ion, but not sufficient to oxidize the relatively more stable bromide ion (Br^-). Some experiments were made by utilizing the electrometric measurement of the oxidation potential. When 1 gram of Chloramine-T[1] was added to 100 cc of a solution having a p_H of 9, the voltage reading (using platinum electrode connected with the positive pole of the galvanometer[2]) was 0.12 V. When 1 gram of Chloramine-T was dissolved in 100 cc of water, having a p_H of 7 (the calomel[3] cell was connected to the positive pole of the galvanometer), the voltage reading was 0.4. When the solution was acidified, the voltage, of course, was increased enormously. Obviously this shows that Chloramine-T is greatly activated as an oxidizing agent when the medium is acid, whereas in alkaline solutions its oxidizing power is lowered proportionally to the concentration of the hydroxyl ions and it even acts as a reducing solution. As the bactericidal power of Chloramine-T is due probably to the oxidizing action (Cl^+), the question of the reaction of the medium is very important. The statement that Chloramine-T is fifty times more active as a germicide than phenol may be entirely wrong in certain media. There is great need for bacteriologic work to determine whether or not in an alkaline solution Chloramine-T has marked antiseptic value such as exists in an aromatic powder containing sodium bicarbonate. In fact from these experiments, it would not be surprising to find that the hydrogen ion concentration (C_H), the oxidation potential and the bactericidal coefficient would be in direct ratio and that Chloramine-T is weakly antiseptic in alkaline solutions. It is hoped that some investigators will take up work along this line.

PURITY OF MARKET SUPPLY OF CHLORAMINE-T AND PREPARATIONS.

The essential standards of purity for Chloramine-T (sodium para-toluene sulphochloramid $CH_3C_6H_4SO_2NaN—Cl^+ + 3H_2O$, 1:4) are described in "New and Nonofficial Remedies." The determinations reported in this paper are (1) loss in weight at 100–102° C., (2) decomposition (melting point), and (3) chlorine content (active chlorine).[4,5] The specimens were purchased on the open market

[1] This sample of Chloramine-T contained no free alkali and its solution reacted neutral to phenolphthalein and to methyl red.

[2] The Wendt Electro-Titration Apparatus was used.

[3] Using normal potassium chloride solution.

[4] It is not uncommon to find chemists using the term "available" chlorine, irrespective of what factor is employed. In these determinations, the actual content of positively charged chlorine is determined, that is, the amount of the active form of chlorine. Available chlorine is calculated on the assumption that the positive chlorine (Cl^+) takes up an atom of negative chlorine (Cl^-) forming a molecule of chlorine, Cl_2 ($Cl^- - Cl^+$). This terminology probably is a hangover from the archaic method of determining the strength of hypochlorites by measuring the amount of chlorine evolved under appropriate treatment in the presence of chlorides. It would seem that the time has come for the Pharmacopœia and books of reference to give analytical figures on the actual amount of the reactive substance and to discard the term "available." Whenever the

in original containers. They were received during the latter part of November and the first of December 1921, and kept in the dark until the analysis was made in June 1922.

Chloramine-T Powder.—All the recent specimens of Chloramine-T contain some free alkali. Of the specimens examined, one of the Squibb samples was considerably below the standard in both chlorine and water, while the other two Squibb samples and the Calco product did not contain the correct amount of moisture. The remaining products more closely approximate the "N. N. R." standards.[1] As may be seen from Table I, the products as found on the market are evidently quite stable.

TABLE I.—CHLORAMINE-T POWDER.

Brand.	Loss in weight at 100° C.	Melting point.	Chlorine (Cl^+) content.
Chloramine-T—Calco (Manufacturers).....	11.4	158	12.2
			12.2
Chloramine-T—Monsanto (Baltimore).....	17.8	163	12.50
			12.50
Chloramine-T—Monsanto (Chicago).....	17.8	162	12.50
			12.50
Chloramine-T—Squibb (Baltimore).....	13.4	169	12.2
			12.2
Chloramine-T—Squibb (Chicago).....	8.4	166	10.9
			10.9
Chloramine-T—Squibb (New York).....	13.9	163	12.7
			12.7
Chlorazene—Abbott (Baltimore).....	18.5	160	11.94
			12.00
Chlorazene—Abbott (Chicago).....	17.3	159	11.66
			11.84
Chlorazene—Abbott (New York).....	17.6	159	12.48
			12.47
"N. N. R.".....	18–20	160–185	12–13

Chloramine-T Tablets.—There are two brands described in "N. N. R.:" Chloramine-T Tablets—Squibb and Chlorazene Tablets—Abbott; each is claimed to contain 4.6 grains of Chloramine-T. The tablets were weighed and then assayed, the results appearing in Table II. The tablets as found on the market are quite satisfactory.

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figures for "available chlorine" are given, the mathematical value is just twice the actual amount of positively charged chlorine present (Cl^+).

[5] The assay methods are as follows:

If 1 gram of Chloramine-T is dried at from 100–102° C. for two hours, it loses not less than 18 per cent. nor more than 20 per cent. (water of hydration).

If about 0.5 gram of Chloramine-T (accurately weighed) is dissolved in 50 cc of water, 10 cc of potassium iodide (10 per cent.) and 5 cc of acetic acid (36 per cent.) added and titrated with tenth-normal sodium thiosulphate, the chlorine content should not be higher than 13 per cent. or lower than 12 per cent. Each cubic centimeter of tenth-normal thiosulphate solution is equivalent to 0.00177 grams of chlorine.

[1] In previous editions of "N.N.R.," the limits of water were 17 to 20 per cent. and of chlorine (Cl^+) from 11.5 to 13.0. On the recommendation of the manufacturers and after consultation the standards were made more stringent: the lower water limit raised to 18 per cent. and the lower chlorine limit raised to 12.0 per cent. The market supply is more in keeping with the old standards than with the revised standards.

TABLE II.—ANALYSIS OF "CHLORAMINE-T TABLETS, 4.6 GRAINS."

Brand.	Weight of tablet. Grams.	Grains.	Amount of Chloramine-T found. Grams.	Grains.
Chloramine-T—Squibb (Baltimore)	0.2995	4.62	0.2911	4.49
	0.2951	4.55	0.2863	4.41
	0.3176	4.89	0.3060	4.72
	0.2901	4.47	0.2850	4.30
Chloramine-T—Squibb (Chicago)	0.2935	4.53	0.3034	4.67
	0.2937	4.53	0.2934	4.53
Chloramine-T—Squibb (New York)	0.2998	4.62	0.3006	4.63
	0.2871	4.43	0.2839	4.38
	0.2826	4.40	0.2818	4.35
Chlorazene—Abbott (Baltimore)	0.3496	5.38	0.2977	4.58
	0.3612	5.57	0.3027	4.65
	0.3477	5.35	0.2906	4.47
	0.3546	5.46	0.2956	4.54
Chlorazene—Abbott (Chicago)	0.3498	5.40	0.2927	4.51
	0.3324	5.12	0.2785	4.28
	0.3348	5.15	0.2816	4.33
	0.3468	5.34	0.2961	4.56
Chlorazene—Abbott (New York)	0.3472	5.35	0.2991	4.61
	0.3484	5.37	0.2991	4.61
	0.3450	5.32	0.2977	4.58
	0.3462	5.33	0.2991	4.61

Chloramine-T Surgical Paste (or Cream).—Chloramine-T Surgical Paste is claimed to consist essentially of 1 gram of Chloramine-T in 100 grams of a base composed approximately of sodium stearate 15 per cent. and water 85 per cent. Three market specimens each of "Chlorazene Surgical Cream" and "Chloramine-T Surgical Paste" were analyzed as follows:

Chloramine-T Paste—Squibb (Baltimore)	0.83% Chloramine-T[1]
	0.81% Chloramine-T
Chloramine-T Paste—Squibb (Chicago)	1.05% Chloramine-T
	1.06% Chloramine-T
Chloramine-T Paste—Squibb (New York)	1.01% Chloramine-T
	1.00% Chloramine-T
Chlorazene Surgical Cream (Baltimore)	1.19% Chloramine-T
	1.18% Chloramine-T
Chlorazene Surgical Cream (Chicago)	1.12% Chloramine-T
	1.17% Chloramine-T
Chlorazene Surgical Cream (New York)	1.14% Chloramine-T
	1.19% Chloramine-T

The variations are not as much as might be expected from a product containing so much water and organic matter. This fact illustrates how a slight alkalinity preserves the Chloramine-T.

Aromatic Chlorazene Powder—Abbott.—According to "New and Nonofficial Remedies," "Aromatic Chlorazene Powder—Abbott" is composed of "chlorazene 5 per cent., sodium bicarbonate 5 per cent., eucalyptol 2 per cent., saccharin 1

[1] Five to ten grams of the paste were transferred to a glass-stoppered Erlenmeyer flask and accurately weighed. Twenty cc of chloroform, 20 cc of potassium iodide solution (10 per cent.), 70 cc of water and 30 cc of acetic acid U. S. P. were added in the order named. The mixture was shaken until the paste had been entirely broken up, then titrated with tenth-normal sodium thiosulphate, using starch solution as indicator.

per cent. and sodium chloride 87 per cent." Three market specimens were analyzed the amount of Chloramine-T present being calculated from the reactive chlorine (Cl^+).

ANALYSES OF AROMATIC CHLORAZENE POWDER.

	Wt. of sample.	Wt. of Chloramine-T.	Per cent.
(Baltimore).....	7.6579	0.3511	4.59
	10.5332	0.4923	4.65
(Chicago).....	5.7615	0.2706	4.69
	7.3941	0.3476	4.70
(New York).....	8.0189	0.3070	3.83
	7.6588	0.2935	3.83

Thus in case of Samples 1 and 2, the amount of Chloramine-T found is only eight per cent. below the amount claimed whereas in Sample 3, the amount is 25 per cent. less than claimed. This result is probably due to poor mixing since the product is quite stable as will be shown later.

Chlorazene Surgical Powder.—This substance is composed of "Chlorazene (Chloramine-T) 1 per cent., zinc stearate 10 per cent. and sodium stearate 89 per cent." Three specimens were analyzed.

ANALYSES OF CHLORAZENE SURGICAL POWDER.

	Wt. of sample.	Wt. of Chloramine-T.	Per cent.
(Baltimore).....	8.6154	0.0803	0.93
	8.7700	0.0811	0.92
(Chicago).....	9.2089	0.1182	1.28
	9.8076	0.1296	1.31
(New York).....	10.6416	0.0098	0.08
	9.8875	0.0084	0.08

This product shows considerable variation—from thirty per cent. over the claimed amount to 92 per cent. below. (A sample, previously unopened, received in 1917 contained no Chloramine-T.) It is evident that certain conditions arise which cause the Chloramine-T to decompose. The product cannot be considered satisfactory from a standpoint of stability.

PURITY OF MARKET SUPPLY OF DICHLORAMINE-T.

As in the case of Chloramine-T, the essential standards for the purity of Dichloramine-T, para-toluene sulphone dichloramid $\left(CH_3C_6H_4SO_2N\langle^{Cl^+}_{Cl^+}\right)$, are described in "New and Nonofficial Remedies." The determinations reported in this paper are (1) melting (decomposition) point and (2) chlorine content ("active chlorin").[1] The specimens were bought at the same time and in the same method as described under Chloramine-T.

Dichloramine-T Powder.—Of the eight specimens examined (the melting points and the chlorine determinations are given in Table III), all of them came well

[1] The chlorine (Cl^+) determination is carried out according to the "N. N. R." method: About 0.1 gram of Dichloramine-T, accurately weighed, is dissolved in 5 cc of glacial acetic acid, 10 cc of 10 per cent. aqueous solution of potassium iodide added and the mixture titrated with tenth-normal sodium thiosulphate. (If the reagents used liberate iodine, the number of cubic centimeters of tenth-normal sodium thiosulphate volumetric required for their decoloration, as determined by a control, should be deducted from the total volume used.) The chlorine content should not be higher than 29.53 per cent. or lower than 28 per cent. Each cubic centimeter of thiosulphate solution is equivalent to 0.00177 gram of chlorine.

within the standards prescribed in "New and Nonofficial Remedies" except one sample of the Squibb product purchased in Chicago; in the latter case the melting point was quite low indicating decomposition, and the chlorine content was substandard; as might have been expected free hydrogen chloride was very perceptible; the other Squibb specimens were of good order. Except for this one instance, the products are all quite satisfactory.

TABLE III.—DICHLORAMINE-T (POWDER).[1]

Brand.	Melting point.	Chlorine (Cl^+) content.
Dichloramine-T—Abbott (Baltimore)	79–80	28.96%
		29.08
Dichloramine-T—Abbott (Chicago)	81–82	29.28
		29.33
Dichloramine-T—Abbott (New York)	81–82	29.24
		29.41
Dichloramine-T—Monsanto (Baltimore)	80–82	29.27
		29.29
Dichloramine-T—Monsanto (Sargents)	79–81	29.18
		29.18
Dichloramine-T—Squibb (Baltimore)	78–80	28.80
		28.78
Dichloramine-T—Squibb (Chicago)	68–69	25.52
		25.70
Dichloramine-T—Squibb (New York)	77–79	28.85
		28.86
"N. N. R." requirement	78–83	28–29.5

Dichloramine-T Tablets.—Only one firms's tablets have been described in "New and Nonofficial Remedies," namely, the Abbott brand. Three original specimens were examined. (See results in Table IV.) The tablets (claimed to contain 4.6 grains Dichloramine-T) are uniform in weight and are within the variations accepted in this form of medication.

TABLE IV.—"TABLETS DICHLORAMINE-T—ABBOTT, 4.6 GRAMS."

	Weight of tablets. Grams.	Weight of tablets. Grains.	Dichloramine-T. Grams.	Dichloramine-T. Grains.
1. Baltimore	0.2950	4.55	0.2916	4.49
	0.3006	4.63	0.2976	4.58
	0.3014	4.65	0.2976	4.58
	0.2975	4.59	0.2934	4.50
2. Chicago	0.2953	4.55	0.2922	4.50
	0.3047	4.69	0.3012	4.64
	0.3025	4.66	0.3000	4.63
	0.2983	4.59	0.2928	4.50
3. New York	0.3000	4.63	0.2970	4.58
	0.2920	4.50	0.2895	4.47
	0.2958	4.56	0.2916	4.49

PURITY OF THE MARKET SUPPLY OF HALAZONE.

Halazone is used almost exclusively in the form of tablets, containing a mild alkaline substance in which the halazone dissolves when water is treated with the tablet. The powder is, therefore, not carried by some firms in regular stock.

[1] The McNeil brand is also described in "New and Nonofficial Remedies." However, our buyers were not able to supply the product. On inquiry, the firm gave the information that their product was sold almost entirely to dispensing physicians, hence, it was not found in the regular drug trade channels.

The specimens received by us from the drug house bore only typewritten labels; in case of one firm no specimen was obtained. The essential standards of purity are the melting point or rather decomposition point and the chlorine (Cl^+) content.[1] Halazone is para-dichloramidosulphone benzoic acid

$$\left(\begin{matrix}Cl^+\\Cl^+\end{matrix}\!\!>\!NSO_2C_6H_4COOH\right).$$

Halazone Powder.—The products of two firms were examined:

Brand.	Decomposition point.	Chlorine (Cl^+) content.
Halazone—Abbott (Chicago)	195	22.96
		23.14
Halazone—Abbott (New York)	194	22.92
		23.11
Halazone—Monsanto	190	24.08
		24.08
"N. N. R." requirement	—	24.00 to 26.2

The Abbott products are slightly low in chlorine content; the one specimen of Monsanto product is just inside the chlorine (Cl^+) limits.

Halazone Tablets.—The tablets of two firms are listed in "New and Non-official Remedies"—"Abbott" and "Squibbs." Each tablet is claimed to contain 0.004 gram ($^1/_{16}$ grain) of halazone, 0.004 gram of sodium carbonate, and approximately 0.1 gram of sodium chloride. Chlorine (Cl^+) determinations yielded the following results, calculated to halazone:

	Amount of halazone in each tablet.
Halazone Tablets—Abbott (Chicago)	0.0030 gram
	0.0030 gram
Halazone Tablets—Abbott (New York)	0.0035 gram
	0.0035 gram
Halazone Tablets—Squibb (Baltimore)	0.0033 gram
	0.0032 gram
Halazone Tablets—Squibb (Chicago)	0.0030 gram
	0.0030 gram
Halazone Tablets—Squibb (New York)	0.0034 gram
	0.0033 gram

The five specimens reported above are 12.5 to 25 per cent. below the amount of halazone claimed; considering how the compound is used, however, the variations are not therapeutically serious.

[1] The following method for chlorine (Cl^+) determination is detailed in "New and Non-official Remedies:" About 0.150 gram of halazone (or in the case of halazone tablets, 30 tablets), accurately weighed, is dissolved in from 50 to 100 cc of water and 10 cc of a 10 per cent. sodium hydroxide solution. Fifteen cubic centimeters of a 10 per cent. potassium iodide solution are added, and the mixture titrated with tenth-normal sodium thiosulphate volumetric solution. (If the reagents used liberate iodine, the number of cubic centimeters of tenth-normal sodium thiosulphate volumetric solution requires for their decolorization should be deducted from the total volume used.) The available chlorine content of halazone should not be higher than 26.26 per cent. or lower than 24 per cent. Each cubic centimeter of tenth-normal thiosulphate volumetric solution is equivalent to 0.00177 grams of chlorine. The theoretical chlorine content of pure halazone is 26.26 per cent.

TABLE V.—STABILITY OF "CHLORAMINES."

		Decomposition point.	Moisture.	Chlorine (Cl^+).
Chloramine-T—Monsanto	Feb. 1918	164–166	18.46	11.94
	Sept. 1918	*163–164*	*16.61*	*11.9*
	July 1922	152	18.05	11.81
Chloramine-T—Calco	Oct. 1917	168–170	16.82	11.67
	Sept. 1918	*158–159*	*15.69*	11.8
	July 1922	(See footnote 1)		....
Chloramine-T—Squibb	June 1918	181	9.0	11.40
	Sept. 1918	*181*	*9.1*	*11.2*
	July 1922	173	9.2	11.1
Chlorazene—Abbott[2] (Received July 5, 1916)	July 1916	Notes	misfiled	....
	Sept. 1918	163		*11.07*
	July 1922	163		11.00
Chlorazene Surgical Powder (Received Dec., 1917)	.....	.....		0.00 (July 1922)
Aromatic Chlorazene Powder (Received August, 1919)	.....	.....		4.72 (July 1922)
Dichloramine-T—Abbott (Received Oct., 1917)	Sept. 1918	*76–78*		*27.62*
	July 1922	69–72		26.51
Dichloramine-T—Calco	Nov. 1917	81–82		28.6
	Sept. 1918	*75–77*		*27.9*
	July 1922	71–73		26.4
Dichloramine-T—Monsanto	Feb. 1918	80–82		29.2
	Sept. 1918	*77–79*		*28.6*
	July 1922	72–74		27.6
Dichloramine-T—Squibb	June 1918	77–79		29.00
	Sept. 1918	*76–79*		*28.3*
	July 1922	68–69		25.0
Halazone—Abbott	Aug. 1917	196		25.9
	July 1922	192		24.4
Halazone—Calco	Dec. 1917	195		25.9
	Sept. 1918	200		*25.8*
	July 1922	204		25.0
Halazone—Monsanto	Dec. 1917			24.9
	Sept. 1918	*198*		*24.2*
	July 1922	204		24.1
Halazone—Squibb	July 1918	204		24.0
	Sept. 1918	...		*23.8*
	July 1922	202		23.2

STABILITY OF THE CHLORAMINES.

From the foregoing discussion, it is evident that Chloramine-T, Dichloramine-T and Halazone, as now found on the market, do not show serious deterioration in

[1] The Calco specimen of Chloramine-T—Calco was sent in a colorless glass container, and kept as the other specimens. On reëxamination at this time, it was found to be entirely decomposed, containing *no* reactive chlorine and melting at 122–123°. All the other specimens were in dark glass as are the market specimens of Calco. This does not reflect at all against the Calco product, but the observation is of academic interest.

[2] Chlorazene was the first product on the American market. Several specimens were examined, at the request of the Committee on Synthetic Drugs, while the product was in the experimental stage. Then when the market specimen was submitted to the Council, it likewise was examined and found to be satisfactory. The exact figures on this latter specimen have been misfiled, but a chlorine determination on the sample was made by Mr. Rabak in 1918, as well as the recent one reported in this paper.

spite of the presence of the relatively unstable form in which the chlorine exists. This does not dispose of the question of stability over a period of years; so, it was opportune to reëxamine samples analyzed when the products were first submitted to the Council and again examined during 1918 by Mr. Wm. Rabak, at that time connected with the A. M. A. laboratory. In the foregoing table (Table V) are given the dates of the analyses and the figures found in the order in which they were made. Those in italics were by Mr. Rabak to whom credit is due. The specimens were kept in the dark, in their original containers, and at room temperature.

It will thus be seen from Table V that samples of Chloramine-T, kept for about five years, show little deterioration. Dichloramine-T deteriorates somewhat, but the decomposition is not of a spontaneous nature. Halazone undergoes little change on standing. Chlorazene Surgical Powder probably does not keep over a long period, the sample (which had not previously been opened) having no Chloramine-T present; possibly the excipient had a slightly acid reaction hastening decomposition. On the other hand, aromatic Chlorazene Powder is stable; this is to be expected in view of the fact that it is an alkaline substance and hence the oxidizing power of Chloramine-T is lessened. Even solutions of Aromatic Chlorazene Powder deteriorate slowly when kept at room temperature exposed to indirect light over a period of weeks.

DECOMPOSITION OF SOLUTION OF AROMATIC CHLORAZENE POWDER.

(Based on Chlorine (Cl^+) Determination.)

Time.	Per cent.
1 hour	0.0
3 hours	0.7
1 day	2.7
3 days	5.0
8 days	7.0
23 days	14.0
4 months	37.0

CONCLUSIONS.

1. The oxidizing power of Chloramine-T is greatly lessened by slight increase in alkalinity of the solution. It is suggested that the bactericidal power may likewise be lessened in alkaline fluids and investigation is needed.

2. The market supply of Chloramine-T was examined. One Squibb specimen was below standard in both water and chlorine, and two Squibb specimens the Calco Chloramine-T did not contain a sufficient amount of water of crystallization. The Monsanto and Abbott products were satisfactory.

3. Chloramine-T Tablets of all firms described in "New and Nonofficial Remedies" were satisfactory.

4. Aromatic Chlorazene powder is stable.

5. Two samples of Chlorazene Surgical Powder (one recent and one old) were very poor; two others were satisfactory.

6. The market specimen of Chloramine-T pastes are satisfactory.

7. On the whole, the market specimens of Dichloramine-T—"N. N. R." are satisfactory, as are the tablets.

8. The market specimens of Halazone examined were slightly substandard.

9. Halazone tablets over 12.5 per cent. to under 25 per cent. of the professed content were found.

10. Chloramine-T and Halazone are sufficiently stable to be kept over a period of five years. Dichloramine-T, on the other hand, decomposes slowly.

CHICAGO, ILLINOIS

SYNTHETIC HYPNOTICS IN THE BARBITURIC ACID SERIES.

BY ARTHUR W. DOX.

The increasing demand for sleep-producing drugs is perhaps one of the characteristics of the restless age in which we now live. Not a year passes but half a dozen new synthetic hypnotics appear in the patent literature and a few of these find their way into the drug market. Most of these fail to meet the claims made by the manufacturers and are soon discarded, and the physicians continue to prescribe the eight or ten more or less familiar drugs that have survived several decades of clinical experience. Meanwhile, the chemical and pharmaceutical laboratories continue their search for the ideal hypnotic, for it must be admitted that none of the hypnotics in present-day use are entirely free from certain objectionable qualities.

Long before our era of chemical and pharmaceutical research the sleep-producing properties of opium and alcohol were widely known. In oriental countries hashish, or cannabis indica, has been used for centuries, but this has never become popular in our western civilization. Among the natural drugs, hyocyamus is perhaps the only other hypnotic of any importance. The first three, opium, alcohol and cannabis, are decidedly habit-forming. As a matter of fact, only a very small percentage of the total consumption of these drugs can be considered legitimate in the sense of being used under circumstances where a physician would feel justified in prescribing them.

Opium, including its chief constituent, morphine and the morphine derivatives —codeine, heroine, etc.—has been both a blessing and a curse to humanity. For the relief of acute pain, especially in post-operative surgery, no satisfactory substitute has yet been discovered. On the other hand, the morphine habit has fastened itself upon thousands of otherwise useful citizens and left them physical and moral wrecks. The discovery of synthethic hypnotics which are now used in a great many cases where morphine was formerly prescribed, represents, therefore, a distinct advance in medical science. It may be said in general that for the relief of insomnia or sleeplessness due to other causes than acute pain, the use of morphine or its derivatives is no longer necessary.

Curiously enough, none of the synthetic hypnotics bears the slightest chemical resemblance to morphine. The exact structure of the morphine molecule is still unknown, but we know that it is far more complex than any synthetic hypnotic thus far used. The presence of a phenanthrene nucleus, an oxygen bridge forming a furane ring, two hydroxyls one of which is phenolic and the other alcoholic, and a nitrogen ring bearing a methyl group, is about all that has been definitely proved of the morphine structure. On the other hand, some of our common sleep-producing drugs are extremely simple and easily synthesized. The difference is not so much in the size as in the compactness of the molecule. For example, morphine has a molecular weight of 285, and luminal, one of the most powerful of our synthetic

hypnotics, a molecular weight of 232; yet morphine contains five cyclic nuclei and luminal only two.

The great advantage of the synthetic hypnotics over morphine is in their lack of injurious effect upon the higher brain centers and in the fact that they are not habit-forming in the ordinary sense. Individuals are occasionally met with who rely to an unnecessary extent upon these drugs, but the habit, if it can be called such, is hardly a physiological craving. For that matter, any drug may be considered habit-forming. Self-medication is one of our favorite pastimes. We have only to call to mind the number of people among our own acquaintance who resort to a dose of aspirin upon every possible pretext. With the exception perhaps of chloral hydrate the ordinary sleep-producing drugs only rarely develop an injurious habit. The reason is probably their lack of effect upon the higher brain centers and their failure to produce sensations of exhilaration or mental exaltation.

In briefly reviewing the history of synthetic hypnotics, we find that chloral hydrate, $CCl_3\,CH(OH)_2$, was the first to be introduced into medicine. Like many others, this substance was known to chemists years before its medicinal properties were discovered. Liebig prepared and described chloral hydrate in 1832 but it was not until 1869 that Liebreich found it to be a hypnotic and in 1874 it was introduced into the British Pharmacopœia. The search for other hypnotics then began. Only those which may be regarded as distinct types and which have come into extensive use will be alluded to in this brief discussion. Paraldehyde, $(CH_3CHO)_3$ made its appearance in 1883; urethane, $C_2H_5OCONH_2$, in 1885; hypnone, C_6H_5-$COCH_3$, in 1886; amylene hydrate, $(CH_3)_2C_2H_5COH$, in 1887; sulfonal, $(CH_3)_2C$-$(SO_2C_2H_5)_2$ in 1888; chloretone, $CCl_3(CH_3)_2COH$, in 1899; and veronal, $(C_2H_5)_2C$-$(CONH)_2CO$, in 1903.

Analogs and homologs of these in which, for example, bromine is substituted for chlorine, or ethyl for methyl, and condensation products with other substances, have made their appearance in great numbers. Many are patented and sold under fantastic names. In practically all cases their therapeutic action is due to a chemical structure represented by one or more of the substances listed above.

As already stated, the ideal hypnotic has not yet been found. Chloral hydrate is regarded by many physicians as habit-forming, and it has a decidedly depressant action on the heart. Urethane, hypnone and paraldehyde are effective only in comparatively large doses and have a disagreeable nauseating taste. Paraldehyde is widely used in hospitals, but is so unpleasant to take that few physicians would risk losing their practice by administering it to private patients. Sulfonal, as well as its homolog, trional, has a tendency to destroy the blood corpuscles. Chloretone and veronal are perhaps the most satisfactory, yet in doses sufficient to produce quick results their action is too prolonged. The ideal hypnotic should have a high "factor of safety," that is, a wide range between effective dose and toxic dose, and thus minimize the danger of over dosage. It should be prompt in its action and free from after effects. It should not interfere with circulation or respiration. And lastly, it should be non-habit forming and at the same time free from disagreeable taste or odor.

Now what is the mode of action of these drugs? Many theories have been proposed but not one of them is entirely satisfactory. As has been stated, they

are unlike morphine in that they do not affect the higher brain centers, their action being probably limited to the central nervous system and the medulla. The most ingenious explanation is known as the Overton-Meyer theory of narcosis. According to this theory the action of synthetic hypnotics is mechanical rather than chemical. Overton found that the effectiveness of these drugs is proportional to their "distribution coefficient," that is, the ratio of their solubility in fats and lipoids to their solubility in water. Nerve tissue is composed largely of fats and lipoids, hence there would tend to be an accumulation in the nerve tissue of such drugs as are more soluble in lipoids than in water. The nervous system thus becomes partially saturated with a foreign substance and its functioning is mechanically retarded. In support of this theory we have the fact that animals in an emaciated condition, in other words, with less adipose tissue to absorb the drug, are more susceptible to hypnotics, also the fact that certain hypnotics, for example veronal, undergo practically no change in the body and are finally exerted unchanged. On the other hand, many substances in the aromatic series for which hypnotic properties might be predicted from their distribution coefficients, have no such action. Possibly, as Traube suggests, surface tension may also be an important factor. Fuchs has pointed out that all of the hypnotics with the exception of the sulfones contain a hydroxyl group, or a carbonyl group capable of tautomerizing to a hydroxyl. The sulfones are the most readily destroyed in the body and their apparent exception may be ruled out on the assumption that a transition product containing a hydroxyl is formed from them. It must be admitted, nevertheless that the action of hypnotic drugs is still as much a mystery as the phenomenon of natural sleep.

A discussion of the various types of hypnotics and their chief representatives would be far beyond the scope of this paper. We shall limit ourselves therefore to the newest type, the veronal series, in which the writer has been conducting investigations during the past three years.

Veronal, also known as Barbital, was introduced into medicine by Fischer and Mering in 1903. It is 5,5-diethylbarbituric acid, $(C_2H_5)_2C(CONH)_2CO$. This substance, like chloral hydrate, was known to chemists long before its physiological action was discovered. It was first prepared by Conrad and Guthzeit in 1882 by the action of ethyl iodide on the silver salt of barbituric acid. For twenty years no further attention was paid to it. Then came the announcement by Fischer and Mering of the remarkable sleep-producing properties of this substance, and a description by Fischer and Dilthey of a far more satisfactory and economical method of preparing it. Various processes for the manufacture of veronal have been patented, but the method originally described by Fischer and Dilthey—the condensation of ethyl diethylmalonate with urea in the presence of sodium ethylate—is the only one that has been successful on a commercial scale.

Like all of Emil Fischer's work this investigation was painstaking and thorough. He prepared a number of homologs of veronal, among which may be mentioned dimethyl, methyl-ethyl, methylpropyl, dipropyl, ethylpropyl, diisobutyl, diisoamyl and dibenzyl-barbituric acids. With increasing size of these alkyl groups the hypnotic effect increases up to a certain point, then decreases. As might be expected, the two extremes, dimethyl and diisoamyl, have very little action, and the intermediate derivatives follow a parabolic curve with dipropyl at the peak.

Diethylbarbituric acid with further substitution on the nitrogen, as for example, 5,5-diethyl-1-methylbarbituric acid was found to be toxic. Replacement of the oxygen in the 2-position by sulphur, as in 5,5-diethyl-2-thiobarbituric acid gave a toxic product, whereas a similar replacement by the imino group, NH, as in diethylmalonylguanidine, gave an inert substance. All of these products, it will be noted carry two alkyl groups on the 5-carbon atom of the pyrimidine nucleus. If only one alkyl is present as in monoethyl or monopropyl-barbituric acid hypnotic action is absent. This is also the case when the barbituric acid ring is opened up, as for example, the ureide of diethylmalonic acid.

The dialkylbarbituric acids which has been almost entirely neglected during the twenty years preceding Fischer's patent now became the subject of feverish research activity particularly in the German laboratories. Patent after patent appeared in rapid succession, mainly of processes for the manufacture of veronal. Most of these processes are roundabout methods of synthesis and could not possibly compete with Fischer's method on a commercial scale.

Among the other dialkylbarbituric acids of therapeutic value for which specific patents have been granted may be mentioned phenylethyl, cyclohexylethyl, diallyl, phenylallyl, dibutyl and isopropylethyl-barbituric acids. Phenylethylbarbituric acid, sold under the names "luminal" and "phenobarbital" is by far the most important of these. It is said to be two and one-half times as powerful as veronal, and is used extensively in the treatment of epilepsy. Whereas the hypnotic effect of veronal is sometimes preceded by a brief period of excitement, luminal manifests its sedative action almost immediately, and for that reason is often used in the treatment of violent cases of insanity and to ward off epileptic seizures. Of the other derivatives just mentioned, the diallyl is about the only one which can be obtained in the market. It is sold under the name "dial." It is undoubtedly a good hypnotic, but the Council of Pharmacy and Chemistry of the American Medical Association has refused to accept it for "New and Non-Official Remedies" because of an overstatement of the manufacturer's claims. The most recent derivative is perhaps isopropylallyl-barbituric acid, known as "allonal." At the present writing, one of our large pharmaceutical houses is about to put isoamylethylbarbituric acid on the market. A discussion of these new derivatives is out of the question because very few data are available except the advertising propaganda. As regards cost of manufacture, none of these derivatives can compete with veronal, especially those containing two different alkyl groups. Superior merits or special uses must be demonstrated if the product is to be a commercial success. This was actually done in the case of luminal, which however, is not a competitor of veronal, but a distinct drug used for special purposes. Butylethylbarbituric acid is on the European market under the name "someryl." It was prepared and described by the writer several weeks before Carnot and Tiffeneau published their description of it. Since the cost of manufacture by any conceivable process would be greater than that of veronal and its action is not essentially different, we did not consider it worth while to apply for a patent.

The study of many other drugs has shown that the physiological action is often due to some particular grouping of atoms in the molecule. A classic example is the synthesis of the local anesthetic procaine based upon a study of the chemical structure of the alkaloid cocaine. Here it was found that the essential groupings

are the benzoyl radical and a tertiary amine. A much simpler derivative containing these two groupings was then prepared and found to be an excellent substitute for cocaine without the habit forming tendencies. Similarly, the ideal hypnotic may eventually be synthesized when we understand fully the structure of the morphine molecule. For the present, however, we are interested in determining the essential grouping to which veronal owes its hypnotic action. First of all, what grouping has it in common with other known hypnotics? Phenylethyl-hydantoin, diethylbromacetylurea, diethylhomophthalimide and phenylethyldiketotetrahydroxazole have, in common with veronal, the grouping CR_2—CO—NH—CO. It is not unlikely that this grouping is a "hypnophore," to coin a word analogous to the familiar "chromophore" of the dye chemist. The alkyl groups (R_2) may of course be varied within a limited range.

One of the alkyls may be a cyclic structure, *e. g.*, phenyl or cyclohexyl, but thus far the other alkyl has invariably been an open chain. Now how would the physiological properties of these dialkylbarbituric acids be affected if the two alkyls were linked together into a cyclic structure? The molecule would then consist of two cyclic nuclei with a single carbon atom common to both; in other words, a *spiro* derivative, a type of compounds of which comparatively few representatives are known. The writer, in collaboration with Lester Yoder, succeeded in preparing several such compounds. The spiro derivative trimethylenebarbituric acid corresponds to methylethylbarbituric acid in which the methyl and ethyl groups are closed into a four-membered ring. Similarly, pentamethylenebarbituric acid corresponds to ethylpropylbarbituric acid with the terminal carbons of the ethyl and propyl groups united into a six-membered ring. To our amazement, both of these derivatives were entirely devoid of hypnotic action. Likewise, the alkylidene-barbituric acids, with a single alkyl group linked to the 5-carbon of the pyrimidine ring through a double bond, as benzylidene-barbituric acid, $C_6H_5CH{=}C(CONH)_2$-CO, are inactive.

We then undertook to vary the urea grouping of the barbituric acid derivatives. By condensing dialkylmalonic esters with amidines instead of urea we obtained a very interesting series of pyrimidines in which the —NH—CO—NH— grouping of the veronal series was replaced by —NH—CR=N—. These also were devoid of hypnotic action. Evidently then the "hypnophore" group referred to above is actually the essential part of the molecule. Even so slight an alteration of the urea grouping as the reduction of the carbonyl to a methylene had been found by Einhorn to destroy the hypnotic properties of veronal.

Another series of dialkylbarbituric acids which we prepared represents the veronal series with a benzyl group in place of one of the ethyls. Since the comparatively recent introduction of benzyl derivatives into medicine as antispasmodics, it occurred to us that the substitution of a benzyl for an ethyl in veronal might give us a derivative with both hypnotic and anti-spasmodic properties. Benzylethylbarbituric acid and a number of its homologs were accordingly prepared. The most active member of the series was the benzylethyl derivative itself. As we anticipated, it was a powerful hypnotic, but contrary to our expectations, instead of being an antispasmodic it was quite the reverse. The narcosis produced in the experimental animals was preceded by tetanic convulsions. Since the publication of this work, our results have been confirmed by Shonle and Moment of

Indianapolis. These startling results led us to a more critical examination of Macht's deductions regarding benzyl therapy. We are now convinced that the supposed "specific benzyl effect" claimed by Macht is simply a higher alcohol effect. With the benzyl attached directly to carbon as in our derivative a hydrolysis into benzyl alcohol is extremely unlikely, whereas in benzyl benzoate and other benzyl esters such hydrolysis readily occurs. On the basis of chemical structure our derivative, with the benzyl attached directly to the carbon of a cyclic nucleus, resembles the alkaloid papaverine, on which Macht based his deductions, more closely than do his benzyl esters. At present we see no possibility of utilizing benzylethylbarbituric acid therapeutically.

Of the various preparations on the market containing dialkylbarbituric acids only those representing salts with bases can be considered chemical compounds. The sodium salt of veronal, for example, appears under the name "medinal." It has the advantage of greater solubility and for that reason can be used hypodermically, but its action is no different from that of veronal. Salts with alkaloids can also be procured, and in these preparations the veronal and the alkaloid exert their specific actions independently. Other preparations, despite the manufacturer's claims to the contrary, are mere mixtures and not chemical combinations. We considered it of interest therefore to determine the effect of combining a dialkylbarbituric acid in a stable union with other substances of known physiological activity. The products represent ethylpropyl- and isoamylpropyl-barbituric acids united through the gamma carbon of the propyl group to diethylamine, ethylaniline, acetanilide and phenacetin, respectively. Acetanilide and phenacetin, for example, are antipyretics and ethylpropylbarbituric acid a strong hypnotic. Preliminary tests showed that mixtures in molecular proportions retained at least the hypnotic action of the barbituric acid. It remained to be determined what the effect would be of uniting the two constituents in a stable union. The synthesis of a typical preparation involved the following steps: Ethyl malonate $\longrightarrow$ ethyl ethylmalonate $\longrightarrow$ ethyl ethylbromopropyl-malonate $\longrightarrow$ ethyl ethylacetphenetidinopropyl-malonate $\longrightarrow$ ethylacetphenetidinopropylbarbituric acid. The final product may be represented by the formula $C_2H_5O.C_6H_4N\ (COCH_3)CH_2CH_2CH_2(C_2H_5)$-$C(CONH)_2CO$. The substance proved to be so stable that even the acetyl group was very difficult to remove by boiling with strong acid or alkali. Animal tests showed that the hypnotic properties of the barbituric acid had disappeared entirely. This we attribute to the insolubility of the substance which prevents absorption and to its great stability which interferes with the liberation of a simple dialkylbarbituric acid by hydrolysis. On the other hand, the corresponding derivative with diethylamine in place of phenacetin was soluble in water but less soluble in organic solvents thus reversing the distribution coefficient required by the Overton-Meyer theory. We believe that in these derivatives a molecular magnitude has been reached considerably beyond that encountered in the ordinary synthetic hypnotics or in morphine itself, without however, acquiring the compactness of the alkaloid molecule.

It will be noted from the foregoing discussion that luminal (phenylethylbarbituric acid) is the only simple disubstituted barbituric acid containing an aromatic radical linked directly to the pyrimidine nucleus. We found that ethylphenoxybarbituric acid, which is luminal with an oxygen inserted between the phenyl

group and the pyrimidine ring was not a hypnotic. Evidently the phenyl must be attached directly to carbon. The question now arises whether the introduction of a second phenyl would increase the physiological activity still further. A search through the literature showed that no attempts have been recorded to prepare such derivatives. The simplest of this type would be 5,5-diphenyl-barbituric acid, *i. e.*, veronal with both ethyls replaced by phenyls. An isomer of this has been described, *viz.*, 1,3-diphenylbarbituric acid, but here both of the phenyls are attached to nitrogen instead of carbon and the substance therefore does not belong to the veronal series. Our attempts to prepare 5,5-diphenylbarbituric acid were unsuccessful owing to the instability of ethyl diphenylmalonate which was used in the final step of the synthesis. We did however, prepare a substituted derivative, namely, di-(*p*-hydroxyphenyl)-barbituric acid, $(HOC_6H_4)_2C(CONH)_2CO$, also its isomer diphenoxybarbituric acid, $(C_6H_5O)_2C(CONH)_2CO$. Neither of these substances showed physiological activity.

An examination of the structure of the synthetic hypnotics commonly used shows that practically all are aliphatic derivatives. Where an aromatic grouping is present, as in luminal and phenylethylhydantoin, the aromatic group comprises a relatively small part of the molecule. On the other hand, aromatic derivatives for which hypnotic properties might be predicted on the basis of their distribution coefficient and molecular stability are generally inert.

Hypnone (acetophenone) perhaps comes the nearest to being an aromatic hypnotic, but a further increase in the aromatic groupings, as in benzophenone and benzhydrol, causes the hypnotic action to disappear. It is of interest to note that the two barbituric acids under discussion consist essentially of two benzene rings and one pyrimidine ring, that is, they are preponderantly aromatic. The hydantoins furnish a parallel case; phenylethylhydantoin, mainly aliphatic, is a hypnotic, while diphenylhydantoin, mainly aromatic, is not. Further evidence is of course required to establish this point, but from the data at hand it would appear that a search for hypnotics among derivatives that are essentially aromatic is not very promising.

Experimental hypnotics must of course be thoroughly tested out with animals before even preliminary tests are made with human subjects. Various animals have been used for this purpose. Fischer and Mering's original experiments with veronal and its homologs were performed with dogs. The more active hypnotics when administered orally in a one gram dose to a dog of average weight cause first a marked muscular incoördination followed by drowsiness and finally sleep which lasts six or eight hours. We found in our experiments that preliminary tests could be performed very satisfactorily with white mice by intraperitoneal injections of either an aqueous solution of the sodium salt or an olive oil solution of the free acid. The advantages of this method are the smaller amount of material required for the test, a great saving of laboratory space and the avoidance of certain disagreeable features always met with in experimentation with larger animals. For example, the effective dose of veronal for a 20-gram mouse is only 0.006 Gm. Within twenty minutes the mouse is in a state of coma which lasts for several hours, after which recovery takes place without any apparent after-effects. This method we have found very useful as a preliminary test to eliminate from further consideration derivatives which are physiologically inert.

From our study thus far of the barbituric acids certain negative data are presented for the purpose of narrowing down the scope of future investigation. The following tentative conclusions may be drawn, supplementary to those of Fischer and Mering.

1. To manifest hypnotic action without undesirable after-effects, the two alkyl groups in the 5-position of the pyrimidine ring should have a total number of carbon atoms not less than four or more than eight.

2. At least one of the alkyl groups must be in the form of an open chain.

3. The benzyl group is undesirable because of its tendency to cause convulsions.

4. The urea grouping —NH—CO—NH— may not be replaced by the amidine grouping —NH—CR=NH—.

5. Increase in the size of the molecule beyond, say, a molecular weight of 250 results in loss of hypnotic activity.

6. Not more than one of the two alkyl groups should be aromatic in character.

7. We believe that the hypnophore group in the veronal series is $—CR_2—CO—NH—CO—$.

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Diethyl	782,739 (1905)	veronal	Phenylallyl	1,056,793 (1913)	
Phenylmethyl	1,025,526 (1912)		Isopropylethyl	1,255,951 (1918)	
Phenylethyl	1,025,872 (1912)	luminal	Dibutyl	1,331,712 (1920)	
Diallyl	1,042,265 (1912)	dial	Isopropylallyl	1,444,802 (1923)	allonal

DEPT. OF CHEMICAL RESEARCH,
PARKE DAVIS & CO., DETROIT, MICH.

PAPER NO. 20.

THE HYDROGEN ION CONCENTRATION OF SOME U. S. P. PRODUCTS.

SHOULD LITMUS BE SUPPLEMENTED BY MORE SENSITIVE INDICATORS?

BY PETER MASUCCI AND MARGARET I. MOFFAT.

The hydrogen ion concentration of certain U. S. P. products was determined electrometrically by means of a hydrogen electrode. These measurements were made on routine samples which were submitted to the Analytical Laboratory to be tested for identity and purity. The solutions of each substance was made

according to the directions given by the U. S. P. under the respective product. In the majority of cases an aqueous solution 1 in 20 was used.

The purpose of this investigation was twofold, (1) to determine the uniformity of reaction of the different lots of the same substance, and (2) to compare the hydrogen ion concentration found, with the statements made in the U. S. P. with reference to the reaction of that substance to litmus. Incidentally, this enabled us to compare the sensitiveness of litmus with the Clark and Lubs phenolsulphonephthalein series of indicators.

The products tested were: (1) Codeine Sulphate, (2) Morphine Sulphate, (3) Quinine Dihydrochloride, (4) Quinine Hydrochloride, (5) Quinine Sulphate, (6) Strychnine Sulphate, (7) Atropine Sulphate, (8) Caffeine Alkaloid, (9) Sodium Glycerophosphate and (10) Sodium Cacodylate.

EXPERIMENTAL.

As previously stated the hydrogen ion concentration of each solution was determined electrometrically. The reaction of each solution was then tested by means of litmus paper or litmus solution, and also by the appropriate Clark and Lubs indicator.

The hydrogen ion concentration is expressed in terms of p_H. The reaction of the solutions to the various indicators is given in terms of the change of color. In order to facilitate the comparison the color change and p_H range of the indicators used are given.

Name.	Color change.	p_H range.
Thymol Blue	Red-yellow	1.2–2.8
Brom Phenol Blue	Yellow-blue	3.0–4.6
Methyl Red	Red-yellow	4.4–6.0
Brom Cresol Purple	Yellow-purple	5.2–6.8
Phenol Red	Yellow-red	6.8–8.4
Cresol Red	Yellow-red	7.2–8.8
Thymol Blue	Yellow-blue	8.0–9.6

The results obtained are given below in Tables I–X inclusive.

TABLE I—CODEINE SULPHATE AQUEOUS SOLUTION 1 IN 40.

Lot no.	Manuf.	Date rec.	p_H.	Litmus paper.	Litmus sol.	Brom Phenol Blue.	Methyl-Red.	Brom Cresol Purple.
4112	"A"	2/12/21	4.81	Neutral	Neutral	Blue	Red	Yellow
4256	"A"	8/8/21	5.15	Neutral	Neutral	Blue	Red	Yellow
5067	"A"	11/12/21	4.90	Neutral	Neutral	Blue	Red	Yellow
5710	"A"	2/23/22	4.61	Neutral	Neutral	Blue	Red	Yellow
6827	"A"	6/12/22	4.53	Neutral	Neutral	Blue	Red	Yellow
9366	"A"	11/11/22	4.56	Neutral	Neutral	Blue	Red	Yellow

TABLE II——MORPHINE SULPHATE AQUEOUS SOLUTION 1 IN 20.

Lot no.	Manuf.	Date rec.	p_H.	Litmus paper.	Litmus sol.	Brom Phenol Blue.	Methyl Red.
4183	"B"	7/5/21	3.67	Faintly red	Faintly red	Blue	Red
4242	"B"	8/5/21	3.80	Faintly red	Faintly red	Blue	Red
4298	"B"	8/11/21	3.80	Faintly red	Faintly red	Blue	Red
4626	"B"	9/23/21	3.76	Faintly red	Faintly red	Blue	Red
5560	"B"	2/2/22	4.28	Faintly red	Faintly red	Blue	Red
5905	"B"	3/5/22	3.94	Faintly red	Faintly red	Blue	Red

TABLE III—QUININE DIHYDROCHLORIDE AQUEOUS SOLUTION 1 IN 20.

Lot no.	Manuf.	Date rec.	P_H	Litmus paper.	Litmus sol.	Thymol Blue.	Methyl Red.
4139	"B"	2/15/21	2.62	Red	Red	Yellow	Red
4274	"B"	8/10/21	2.79	Red	Red	Yellow	Red
4651	"B"	9/7/21	2.74	Red	Red	Yellow	Red
5934	"B"	3/17/22	2.70	Red	Red	Yellow	Red
7981	"C"	9/2/22	2.59	Red	Red	Yellow	Red
9924	"C"	12/7/22	2.45	Red	Red	Yellow	Red

TABLE IV—QUININE HYDROCHLORIDE AQUEOUS SOLUTION 1 IN 20.

Lot no.	Manuf.	Date rec.	P_H	Litmus paper.	Litmus sol.	Methyl Red.	Brom Cresol Purple.
2960	"B"	5/27/21	5.92	Neutral	Neutral	Yellowish red	Purple
4146	"B"	7/18/21	5.70	Neutral	Neutral	Yellowish red	Purple
4881	"B"	10/25/21	5.93	Neutral	Neutral	Yellowish red	Purple
5418	"B"	1/3/21	5.83	Neutral	Neutral	Yellowish red	Purple
6742	"C"	6/5/22	5.60	Neutral	Neutral	Red	Greenish yellow

TABLE V—QUININE SULPHATE AQUEOUS SOLUTION SATURATED.

Lot no.	Manuf.	Date rec.	P_H	Litmus paper.	Litmus sol.	Methyl Red.	Brom Cresol Purple.
4912	"B"	10/27/21	5.79	Neutral	Neutral	Reddish yellow	Yellowish purple
10769	"C"	2/2/23	5.66	Neutral	Neutral	Reddish yellow	Yellowish purple
10988	"C"	2/16/23	6.34	Neutral	Neutral	Reddish yellow	Yellowish purple
11091	"D"	2/22/23	5.24	Neutral	Neutral	Red	Yellow
11179	"B"	2/27/23	5.12	Neutral	Neutral	Red	Yellow
11228	"C"	2/16/23	5.49	Neutral	Neutral	Red	Yellow

TABLE VI—STRYCHNINE SULPHATE AQUEOUS SOLUTION SATURATED.

Lot no.	Manuf.	Date rec.	P_H	Methyl Red.	Brom Phenol Blue.	Brom Cresol Purple.	Litmus paper.
4872	"E"	10/22/21	4.48	Red	Blue	Yellow	Neutral
6041	"E"	3/27/22	5.07	Red	Blue	Yellow	Neutral
6267	"E"	4/20/22	4.98	Red	Blue	Yellow	Neutral
6825	"E"	6/12/22	4.48	Red	Blue	Yellow	Neutral
6946	"E"	6/20/22	4.48	Red	Blue	Yellow	Neutral
10441	"E"	1/12/23	4.73	Red	Blue	Yellow	Neutral

TABLE VII—ATROPINE SULPHATE AQUEOUS SOLUTION 1 IN 20.

Lot no.	Manuf.	Date rec.	P_H	Brom Phenol Blue.	Methyl Red.	Brom Cresol Purple.
4345	"E"	8/19/21	4.39	Blue	Red	Yellow
4939	"E"	10/41/21	5.66	Blue	Red	Purple
5371	"F"	12/20/21	6.67	Blue	Reddish yellow	Purple
5583	"F"	2/6/22	6.20	Blue	Reddish yellow	Purple
5944	"F"	3/10/22	6.08	Blue	Red	Purple
6366	"E"	5/1/22	4.48	Blue	Red	Yellow

TABLE VIII—CAFFEINE ALKALOID AQUEOUS SOLUTION SATURATED.

Lot no.	Manuf.	Date rec.	P_H	Brom Cresol Purple.	Phenol Red.	Brom Thymol Blue.
5184	"H"	11/23/21	5.91	Yellow	Yellow	Yellow
5433	"A"	1/5/22	4.98	Yellow	Yellow	Yellow
11008	"G"	2/16/23	7.35	Purple	Yellow	Blue

TABLE IX—SODIUM GLYCEROPHOSPHATE AQUEOUS SOLUTION 1 IN 20.

Lot. no.	Manuf.	Date rec.	p_H.	Phenol Red.	Thymol Blue.	Cresol Red.
4048	"H"	7/1/21	8.57	Red	Blue	Red
5703	Unknown	2/22/22	8.19	Red	Yellowish blue	Red
7180	"H"	7/6/22	8.11	Red	Yellowish blue	Red
7394	"H"	7/24/22	8.70	Red	Blue	Red
8266	"H"	9/18/22	8.74	Red	Blue	Red
9939	"H"	12/8/22	8.65	Red	Blue	Red

TABLE X—SODIUM CACODYLATE AQUEOUS SOLUTION 2 GM. IN 50 CC.

Lot no.	Manuf.	Date rec.	p_H.	Phenol Red.	Cresol Red.
4618	"I"	9/22/21	7.69	Red	Yellow
5092	"I"	11/16/21	7.69	Red	Yellow
8761	"A"	10/10/22	8.03	Red	Red
9540A	"I"	12/21/22	7.86	Red	Red

DISCUSSION OF RESULTS.

The results given in the tables are self-explanatory but in order to emphasize some of the points a couple of the substances tested will be discussed in detail.

(1) *Codeine Sulphate.*—The average p_H of six samples was 4.76. The p_H range was 4.53–5.15 or a difference of 0.62 p_H. The significant point to be noted is that all the samples were distinctly acid in reaction in reference to the true neutrality p_H 7.0. Yet they failed to change litmus paper or solution, that is, they were neutral to this indicator. This finding agrees with the statement in the Pharmacopœa—namely, that a solution of Codeine sulphate 1 : 40 is neutral or not more than faintly acid to litmus. When the solution is tested with more sensitive indicators, one finds that it is on the alkaline side of Brom Phenol Blue and on the acid side of Methyl Red and Brom Cresol Purple. These indicators, therefore, denote at once the true reaction of the solution.

(2) *Morphine Sulphate.*—The average p_H of six samples was 3.88. The p_H range was 3.67–4.28 or a difference of 0.61 p_H. This preparation was found to be slightly acid to litmus which again agrees with the statement made in the Pharmacopœa that a solution of Morphine sulphate 1:20 is neutral or slightly acid to litmus. It must be borne in mind, however, that a p_H of 3.88 is more acid than solution of $N/1000$ acetic acid and therefore the phrase "neutral or slightly acid to litmus" does not mean much. On the other hand the use of Brom Phenol Blue or Methyl Red would give the true reaction of the solution.

What has been said about Codeine Sulphate and Morphine Sulphate applies to the other substances tested. The use of litmus should be discontinued or at least supplemented by the more sensitive indicators. The litmus of commerce is of uncertain composition and is contaminated with impurities. Its degree of sensitiveness is not certain and is bound to vary. There is no doubt but that synthetic indicators are far superior. This class of indicators has for the most part displaced litmus especially in bacteriological work.

The writers are of the opinion that the Clark and Lubs series of indicators should be included in the next Pharmacopœa not only to determine the degree of acidity or alkalinity (hydrogen ion concentration) but also in certain titrations of alkaloids. Already Lizius and Evers[1] have studied the question of the use of indicators in the titration of acids and bases. They conclude that "the indis-

criminate use of phenolphthalein for all weak acids and of methyl orange for all weak bases cannot and does not give results of such accuracy as may easily be obtained if the right indicator is used."

McGill[2] determined the hydrogen ion concentration of certain alkaloidal salts by the potentiometer method. From the values obtained he chose the indicator which would give the most accurate results. He pointed out the greater accuracy of some of the phenolsulphonephthalein series of indicators.

The writers are also of the opinion that the new U. S. Pharmacopœa should include in Part II General Tests, the colorimetric method outlined by Clark[3] for the determination of hydrogen ion concentration. It should prove as useful for the pharmacists as it has for the biologists in the investigation of phenomena which is seriously influenced by the p_H of the solution.

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ON THE CALCIUM ION.

BY R. A. KUEVER.

It has long been known that calcium ion is of value in checking diarrhea. Taken in excessive quantities it produces constipation. Prepared chalk, which when taken into the stomach and converted into calcium chloride, is extensively used to control diarrhea and dysentery. Chalk is an effective antacid and valuable in the treatment of gastric hyperacidity. The objection to its continued use, however, in such cases, is the constipation that results. Magnesium carbonate, the antacid so commonly employed in gastiric hyperacidity, is distinctly laxative. And where this is objectionable, as it often is, the two carbonates may be administered mixed in equal proportion, thus producing neither a laxative nor constipating, but merely the antacid effect. No matter what calcium salt is employed, constipation follows—the more soluble salts being more efficacious than those which dissolve but sparingly. And while chalk, *per se*, is insoluble, it is converted to a very soluble form (calcium chloride) the moment it comes in contact with the hydrochloric acid of the gastric juice.

The value of calcium ion in the circulation, in order that blood may have a normal coagulating index, has also been known for some time. Thrombin causes blood to coagulate by converting dissolved fibrinogen into insoluble fibrin. Pope believes that the change takes place as follows: when the blood leaves the body, one of its constituents (probably the leucocytes) gives rise to a pro-enzyme, which is converted into the active enzyme under the influence of calcium ion. Gurber says that acid calcium phosphate is dissolved in the fluids of the body and that the calcium ion aids in the formation of fibrin ferment.

It is now a matter of common practice for surgeons to determine the coagulating index of the blood preceding operations. In case it is found to have a low coagulating index, the patient is given doses of calcium salt repeatedly until the coagulating index has become normal or at least materially increased. Serious hemorrhages are frequently avoided in this way. Of particular importance in this connection with mastoid, tonsil, or other operations in which there is danger of serious hemorrhages. In this respect the calcium ion is considered as a hemostatic and it is probably the only substance known which will increase the formation of fibrin ferment.

The proper coagulating index of blood is an important matter also, in so far that the blood clot, when normally and quickly formed, seals the wound and protects the granulation tissue. In this way it also prevents infection.

Another important function of the calcium ion in the human body, is that it increases phagocytosis. In fact, Fischer and Riethmuller have concluded that, besides calcium ion, no other substance is capable of increasing the phagocytic action of the leucocytes. Hamburger has found that while calcium has a stimulation function on the heart, sodium exerts marked toxic effects. And Sticker has demonstrated that the phagocytic action of the leucocytes is also impaired by the toxic action of sodium, but stimulated by calcium. Chiari and Januschke have found that the calcium salts have a remarkable action in reducing inflammation of tissues. Leo substantiates their findings and regardless of the bacteria selected his results were all positive. His conclusion was that the calcium ion does not exert an influence against the phlogogenic organisms, but serves to strengthen the resistance of the tissues against the influence of these bacteria.

Gurber, after experimenting for years with the action of calcium ion upon the blood, added to injected solutions, found that it is of prime importance in increasing the resistance of tissues to infections diseases. He found calcium chloride measurably increased phagocytosis in weak solutions (0.01 per cent.) in which solution it is completely ionized. The more concentrated solution he found less effective—in fact, excessive amounts decreased again the phagocytic action of the leucocytes.

From these interesting findings it will be seen how inportant it is to maintain an equilibrium between calcium assimilation and elimination. Moreover, it is easily seen how calcium malnutrition will produce such conditions as rickets, osteitis, osteomalacia, osteomyelitis, dental decay and many other diseases. The extreme prevalence of dental decay may, to some extent, be accounted for by the present-day diet from which calcium compounds are largely eliminated by modern methods of preparation. Investigations by Sherman, Bunge, Kellogg and others indicate that a very large percentage of the civilized race is suffering from calcium starvation because many people are eliminating each day more calcium compounds than they take into the system with their total daily food supply.

Again, from the above findings, it will readily be seen how valuable soluble calcium salts are in treating inflamed tissues. Particularly is this true in dentistry in treating irritated and inflamed gum tissue. Calcium ion increases the resistance of the gums to phlogogenic organisms. It increases the coagulating index of the blood and it causes the immediate formation of blood clots to seal the wounds, to protect granulation tissue and to prevent infection.

For this reason calcium chloride, in the proper dilution, is a very important

ingredient in tooth paste and mouth washes. It is a hemostatic and antiphlogistic. It reduces inflammation and overcomes bleeding gums. Moreover, it does not introduce into the mouth foreign ions, for both calcium and chloride ions are found in normal saliva.

Now that dental investigators are agreed that tooth pastes and mouth washes must be mildly acidic in reaction, calcium chloride may easily be incorporated with marked beneficial results. In fact, dentists should insist that their patients be supplied with dentifrices and mouth washes containing this important salt. Tooth pastes and mouth washes containing the proper amount of calcium chloride have been found noticeably efficacious in overcoming bleeding gums.

The fact that science has proven that mouth preparations must be mildly acidic is rather coincidental in this connection, for calcium chloride cannot be incorporated in alkaline preparations. Being an acid salt—a combination of a strong acid and a weak base—alkalies, particularly soaps, decompose it and destroy its action.

THE USE OF PRECIPITATED COPPER FOR STERILIZING PURPOSES.*

BY GRETCHEN SPRECHER.

It has been known for some time that copper and its salts acted as efficient agents in destroying bacteria, algae, and related minute organisms found in water. Copper sulphate in high dilution (1–500,000 to 1–4,000,000) has proven very efficient in ridding water supplies of annoying accumulations of filamentous algae. As applied in Stowe Lake, Golden Gate Park, San Francisco, enough copper sulphate to make 1–1,000,000, was placed in gunny sacs which were tied to boats and rowed about the Lake until all of the copper salt had gone into solution. As if by magic the filamentous algae disappeared, which until then required the constant labors of a number of men to rake out and dispose of the growth. According to a report by the Bureau of Chemistry this method has proven efficient in ridding city water supplies of algal growths.

In the experiments herein recorded, precipitated copper was used. This material is prepared by passing a current of hydrogen over finely powdered copper oxide, reducing the oxide to metallic copper which is nearly black in color and consists of very minute particles of irregular form. There are on an average 1,840,000 particles of copper per gram. The particles average 25 microns in diameter. Naturally, this reduction in size results in an enormous increase in surface exposure per unit mass of the metallic copper. Considering each particle as a sphere it was estimated that one gram of the copper represented a surface exposure of approximately 3.60 square meters.

Metallic copper when placed in water and in the presence of electrolytes, gives up colloidal copper particles to the water, and it is these colloidal particles of metallic copper which are effective as destroyers of the microörganisms which may occur in such waters. The rate of colloidal diffusion into a liquid as water, in the presence of a given quantity of electrolyte, is directly proportional in the surface exposure of the copper present. It therefore follows that precipitated copper with its enormous surface exposure will yield a maximum amount of colloidal

* Scientific Section, A. Ph. A., Cleveland meeting, 1922.

copper particles within a minimum period of time, and its germ-destroying power is far greater than that of copper in any other form. However, as suggested, the rate of the colloidal diffusion of metallic copper within a given liquid also depends on the amount of electrolyte present. All waters, excepting pure distilled water, contain some electrolyte, and usually enough to yield a sufficient amount of copper for sterilizing purposes. No doubt the efficiency of the copper could be increased and regulated through the addition of some cheap and harmless electrolyte, should the water to be sterilized not contain enough of such substance.

The experimental part of the work was carried out as follows. To 50 cc of average samples of tap water was added 0.1 gram of precipitated copper, making a dilution of 1–500. The mixture was shaken by tapping the container against the palm of the hand (mechanical agitators would be an advantage), and plate cultures made at different periods of time, using the clear supernatant liquid from the top. The controls showed that the tap water in question contained 300 bacteria per cc. The same water exposed to the precipitated copper in the above dilution was free from living bacteria after an exposure of 2 minutes. The test was repeated a number of times and in each instance the results were the same. A few colonies appeared in some of the test plates, but most of these were traceable to accidental contaminations due to the imperfection of the method employed. The results however warrant the conclusion that precipitated copper in the presence of electrolytes is a very efficient destroyer of microörganisms. Incidentally it may be noted that copper has been used with success in the treatment of abscesses, ulcerations, in tuberculosis of the skin, in eye infections, and it is believed to be the active ingredient of some of the secret cancer pastes. According to an article in the *Lancet*, "Brass Paste," which is a combination of copper sulphate, zinc sulphate and picric acid, is very effective in lupus or skin tuberculosis and to reduce tubercular glands. It is suggested that the effects produced are due to colloidal copper.

The manner in which colloidal copper produces its effects is probably as follows. Such solid particles as may appear in a liquid containing the colloidal copper, adsorb said copper particles, and the amount (per unit mass) so adsorbed is proportional to the surface exposure and the electric conductivity of the particle in suspension. Thus a very minute particle will adsorb proportionally more copper than a larger particle possessing the same or like electric conductivity. It thus follows that a microbe may adsorb enough copper to destroy life, whereas a larger organism, as crustacean, fish, lily, etc., cannot possibly adsorb enough copper to do serious harm or to produce appreciable effects of any kind. Just how the adsorbed copper produces death of the cell plants is not determined.

The above brief experiments suggest the possible use of precipitated copper for the purpose of sterilizing drinking water supplies. This might be done by making filtering material consisting of precipitated copper suspended in some inert material as sand, through which the water may percolate. Perhaps copper sponge might be used through which the water would flow readily, thus doing away with the need of a suspending material. Water will not pass through pure precipitated copper as the smallness and the proximity of the particles holds the water by capillarity and will not permit it to flow excepting under considerable pressure.

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A NOTE ON THE SIMULTANEOUS ESTIMATION OF MINUTE QUANTITIES OF SULPHUR AND PHOSPHORUS.*

BY FREDERICK W. HEYL AND BRYANT FULLERTON.

In 1910, Wolf and Österberg[1] described a method in which the substance is oxidized with a large excess of nitric acid in a Kjeldahl flask, and then evaporated to dryness in the usual manner with Benedict's reagent. After ignition over a flame, the residue is taken up in dilute hydrochloric acid and barium sulphate is precipitated and weighed. The excess of barium is removed from the filtrate and phosphorus determined by Neumann's method.

We carried out a few experiments, modifying this method in order to observe if it would be possible to utilize benzidine as the precipitant. In analyzing an organic substance containing 1% of sulphur, the use of a 1.0 gram sample will yield 73 mg. of barium sulphate. If the quantity taken is 0.20 Gm. (= 2 mg. sulphur) the barium sulphate weighed would amount to 0.0146 Gm. If benzidine could be used, one would require for 2 mg. sulphur 6.25 cc $N/50$ alkali to neutralize the benzidine sulphate (1 cc $N/50$ = 0.00032 Gm. sulphur) Raiziss and Dubin[2] have described a method which involves titrating the benzidine sulphate with $N/10$ $KMnO_4$ solution. Here 1 cc $N/10$ $KMnO_4$ is equivalent to 0.001 g. sulphur, making it about three times as delicate as the regular titration with alkali.

Since the methods for the estimation of phosphorus in quantities from 0.1 to 1.0 mg. are well known, it appeared that we might be successful in the determination of both sulphur and phosphorus even if very small samples were employed. MacArthur[3] describes a method for the analysis of the lipin extract of tissues, in which the material approximately (0.08 Gm.) is fused with 5 cc of a 20% solution of potassium hydroxide and sodium nitrate (4–1). Of the final solution 1/5 (0.016 Gm.) served to estimate sulphur by the benzidine method. This method is further discussed but no experimental work is given to show what accuracy might be expected with it.

It seemed needless in our work to take such small quantities as those mentioned by MacArthur. Furthermore the known proved methods do not appear to justify them.

The work described in this paper was carried out for the purpose of determining (1) the accuracy with which 1 mg. of organic sulphur might be determined; (2) the effect of the method employed on the subsequent application of Raper's method on the filtrate.

It was found that, when the alkaline fusion method (Na_2O_2) is employed, that the use of the regularly required amount of fusion mixture prevents the quantitative precipitation of benzidine sulphate. The use of Benedict's solution in place of the fusion mixture also fails to permit the use of benzidine, although the error is much smaller. One must, therefore, rely on the barium sulphate precipitation, as first suggested by Wolf and Österberg. We prefer the fusion method for the analysis of lipins.

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* Received May 25, 1923.

[1] *Biochem. Zeitschrift*, 29, 429, 1910.

[2] *J. Biol. Chem.*, 18, 300, 1914.

[3] *Jour. Am. Chem. Soc.*, 41, 1232, 1919.

Raper's method was not unfavorably influenced by this preliminary determination of sulphur.

EXPERIMENTAL.

The material analyzed was casein. It was first analyzed for phosphorous by the regular fusion method, *i. e.*, 1 Gm. casein + 5 g. Na_2CO_3 + 5 Gm. Na_2O_2 with subsequent addition of 5 Gm. Na_2O_2. The solution was acidified with nitric acid, concentrated to a volume of 200 cc. The molybdate was precipitated as usual and the phosphorus weighed as $Mg_2P_2O_7$. Found, P = 0.80, 0.80%. The above analysis was repeated by Neumann's method.[1] Found, 0.76, 0.75%.

A quantity 0.2 Gm. (= 1.6 mg. P) was ashed by the regular procedure, using 10 cc of nitric + sulphuric acids (1–1). Five cubic centimeters was first added, and the mixture boiled until free from the oxides of nitrogen. Then 3 cc was added, and the mixture boiled further. Then 2 cc further was added and the mixture boiled to a volume of 4 cc. Water (20 cc) was added and the mixture boiled for ten minutes. The solution is made up to 100 cc using 24 cc of ammonium nitrate solution (190 Gm. in 300 cc). The solution is heated to 80° and precipitated with 8 cc of 10% ammonium molybdate solution. The solution is shaken and held in the bath for 20 minutes, with occasional shaking. The mixture is cooled in the ice-bath, 8 cc of 50% alcohol is added, and then filtered through a 7 cm. filter. The precipitate remaining in the flask is washed out by means of ice cold 50% alcohol and the precipitate on the filter paper washed with dilute alcohol until the washings are free from acid, 7 to 8 washings usually sufficing.

The precipitate is then dissolved on the filter paper, by dropping N/20 sodium hydroxide solution on it, from a burette, care being taken to have an excess not exceeding 2 or 3 cc. The filter paper is thoroughly washed with water until free from alkali. The volume should be about 175 cc. The solution is boiled down to 100 cc to remove ammonia. Phenolphthalein test solution (0.5 cc) is added and the solution titrated with *N*/20 sulphuric acid solution, 2 cc excess being added. The solution is then boiled to remove carbon dioxide. After removal of CO_2, the solution is titrated to a light pink color with *N*/20 alkali. (1 cc *N*/20 sol. = 0.0553 Mg. phosphorus.)

When 0.10 Gm. casein was taken, and the entire operation conducted proportionately the same result was obtained.

By Raper's[2] method, using 0.2 Gm. samples, we obtained 0.81% P.

Sulphur Determinations.—Several estimations were made by the regular fusion method using 1.0 Gm. samples. Found: 0.69, 0.71, 0.68%.

Effect of Benedict's Reagent on Precipitation of Benzidine Sulphate.—A standard solution of K_2SO_4 was prepared by dissolving 5.4438 Gm. in 1 liter. (1 cc = 1 mg. S.) This solution was diluted 1:10 for the following work, so that 10 cc = 1 mg. S.

Fifteen cc (1.5 mg. S) was transferred to a wide mouth flask. The solution was acidified with normal hydrochloric acid. Benzidine hydrochloride solution[3] (25 cc) is added and a few cubic centimeters of acetone. After standing, the precipitate was filtered on a Gooch, washed with ice cold 50% acetone, and then titrated (*a*) with *N*/50 sodium hydroxide[4] and (*b*) with an approximately *N*/10 potassium permanganate solution.

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[1] Kleinmann, *Biochem. Zeits.*, 99, 95, 1919.

[2] *Biochemical Journal*, 8, 649, 1915.

[3] Made by dissolving 6.7 Gm. benzidine in 29 cc hydrochloric acid (1.12) and diluting to 1000 cc.

[4] *J. Biol. Chem.*, 47, 63, 1921.

Taken.	Cc $N/50$ NaOH.	Cc $KMnO_4$ used.	1 cc $KMnO_4$.
1.5 mg. S	4.5	13.85	0.0001083 Gm. S
1.5 mg. S	4.5		
1.0 mg. S		9.0	0.000111 Gm. S
		8.9, 9.1	

The above work was repeated, first evaporating the solution to dryness, and oxidizing with 5 cc Benedict's reagent. After igniting and taking up in hydrochloric acid (1:4) the solution was almost neutralized and the benzidine precipitation carried out as before. The following results are typical.

Sulphur taken.	Cc $N/50$ alkali.	Cc $KMnO_4$ used.	Error.
1.0 mg.	2.8	8.3	−8%
1.5 mg.	4.5	13.65	
	4.45	13.8	
	4.4	13.9	
	4.35	12.9	−7%

The use of Benedict's reagent in amounts of 5 cc per 1 mg. of sulphur gave results which while not sharp were tried on Casein. This substance was boiled with 5 cc HNO_3, then 3 cc fuming acid was added and finally 2 cc. After boiling, the solution was transferred to a small casserole and evaporated to dryness with 5 cc Benedict's reagent. (Less cannot well be used.) The analysis was completed as above described.

Casein taken.	Cc $KNnO_4$ required.	S found mg.	% Sulphur.
0.2000	12.5	1.35	0.68
	12.9	1.40	0.70
	12.45	1.35	0.675
	12.1	1.31	0.66
	12.15	1.32	0.66
	12.3	1.35	0.665
	13.3	1.44	0.72

These results[1] indicate the accuracy which may be expected under these conditions, but they are less accurate when more Benedict's solution is required, or when less sulphur is present. Furthermore in the analysis of lipins there is a greater tendency to loss by puffing than with casein.

When the analysis is carried out exactly as before except that $BaSO_4$ is precipitated and weighed, 1.29 to 1.32 mg. sulphur was found, *i. e.*, 0.65–0.66%.

As a result of our experience we prefer the fusion method. 0.2 Gm. was fused with 1.0 Gm. Na_2CO_3 + 1. Gm. Na_2O_2 and then a second 1. Gm. Na_2O_2 was added. By this method 1.37 mg. sulphur (0.685%) was found.

Using the regular fusion method, we found that benzidine cannot be employed as the precipitant when a requisite amount of alkali is used.

Determination of Phosphorus in Filtrates.—The influence of copper or the sodium salts is negligible. The excess of benzidine or barium was removed with sulphuric acid and 5 cc conc. H_2SO_4 added to filtrate. The analysis when com-

[1] Occasionally the variation exceeds that shown in this table owing to the failure of the benzidine sulphate to crystallize. In these analyses the precipitation mixture stood in the ice-chest over night. For example the duplicate with analysis 5 required only 11.05 cc $KMnO_4$ (0.60%). A number of attempts were made to secure more perfect precipitation through the addition of 10 cc standard K_2SO_4 solution, just before adding the benzidine. Results as low as 0.61% have been recorded with this modification.

pleted by Raper's method gave 0.80, 0.82, 0.775, 0.78, 0.74, 0.81,[1] 0.80,[1] 0.78, 0.81%.

SUMMARY.

Small quantities of sulphur (1 mg.) in organic substances can be determined by the fusion method, by weighing barium sulphate as accurately as with the benzidine method, using Benedict's reagent. For lipins the fusion method is preferable because the chance of loss by puffing is eliminated.

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THE BIOLOGICAL TESTING OF SALVARSAN AND ITS DERIVATIVES.*

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In the armamentarium of the modern physician certain compounds of arsenic have a very important position. This position has been gained by the clinical and experimental evidence which has accumulated during the past eighteen years since the announcement of the discovery of Salvarsan by Ehrlich. While compounds of arsenic were used prior to this and hundreds have been synthesized and tried in the treatment of disease since then, none have equalled Salvarsan and Neosalvarsan for use in the treatment of syphilis.

The properties which the physician seeks are purity, complete solubility, relative non-toxicity and therapeutic efficiency. These properties are controlled by the manufacturer in his laboratories before the product is offered to the physician. For this purpose he maintains a staff of chemists and biologists, the first to conduct the chemical and physical tests, the second to test the product for its toxicological and therapeutic properties by the modern scientific methods which have been developed for these purposes. These methods are the result of the investigations of workers in Government and private laboratories both in this country and abroad. The early work of Ehrlich and Hata in Germany has been followed by that of Dale in England, Danysz in France and Voegtlin and others in the United States. This laboratory has carried on such biological tests since the advent of Salvarsan as an American made product. It is this type of studies that has given Salvarsan and Neosalvarsan uniform reliability without sacrificing therapeutic activity. Another factor contributing to the uniformity of these products is their manufacture on a large factory scale rather than a number of small lots such as are made in smaller laboratories.

In order that a compound shall have value in the treatment of a disease it is necessary that it be tolerated by the animal body in a much larger amount than is required to kill the micro-organism which is the causative factor in this disease. It is obvious that if quinine were tolerated by the plasmodium of malaria in larger amounts than can be borne by man, quinine would never have been used in the treatment of this infection. So, in the field of organic arsenicals, those compounds are discarded which have a curative dose approaching the tolerated

[1] 0.1 Gm. samples.

* From the Laboratory of Biological Testing, H. A. Metz Laboratories, Inc., 644 Pacific St., Brooklyn, N. Y.

dose or lethal dose. It is the function of the biologist to determine, in searching for new drugs, as nearly as he may the range between these doses; as a control test on the established specifics, to determine that the product does not depart from the standards established for a satisfactory preparation intended for the treatment of human disease.

The standards for the control of the manufacture and testing of Salvarsan and its derivatives have been promulgated by the U. S. Public Health Service under Act of Congress, 1902, and in addition to the tests made by the manufacturer, samples of all lots made for sale are submitted to the Hygienic Laboratory for additional tests, both chemical and biological.

In this country, the biological tests, both for toxicity and therapeutic value, are made upon white rats. In England, Canada, and Germany, white mice are used by many workers. It is probable that the uniformity of the animals used is of more importance than the species chosen. The test for toxicity of the product, or for the maximum dose of the product which is tolerated by the test animals, consists in observing, for a certain period, animals which have been injected with definite amounts of the drug. The period of survival is noted. Autopsies are made and the condition of the organs noted in case of death. The survivors are killed at the end of the test period and examined. The test period for Salvarsan is 48 hours; for Neosalvarsan, 7 days. Various factors are of importance in attaining standard conditions for these tests and these will now be described briefly.

As has been pointed out by Lake and others, the care of the animal is of fundamental importance. The rats must be free from disease, must have an adequate diet, plenty of clean water and must be kept under favorable conditions of temperature and ventilation in clean cages. These conditions can be secured by the proper selection of the articles of diet to include the necessary proteins, carbohydrates, mineral constituents and vitamines; a competent and trustworthy assistant completes the requirements which one should have before attempting to test these products.

The rats are kept on a standard, dry food diet with plenty of clean water for at least a week before use. Weights on the animals are taken at the beginning and end of the period of observation. Those which have shown a normal rate of growth are selected as fit for use. Since the preparations are given on a weight basis, the animals are deprived of food for twelve to eighteen hours before weights are taken. In order to obtain a further idea of the effect of the drug, weights are taken at the end of the period of observation following the injection of the drug.

The drugs are given in an aqueous solution which is injected into the saphenous vein, *at a definite rate*. As has been shown by Lake, too rapid injection increases the apparent toxicity of Salvarsan. Myers points out that the rate of injection has an effect on the size of the protein-salvarsan aggregate formed in the blood stream and so affects the toxicity directly. Skilled assistance and gentle handling of the animals during the injection contribute to the constancy of results.

The *preparation* of the solution before injection is of *extreme importance*. The *concentration, temperature, effect of shaking, age of solution*, and, in the case of Salvarsan, *the amount of alkali* added *are all factors in determining the toxicity of a given product*. A concentration of 2% is used in testing Salvarsan and Silver

Salvarsan; one of 4% for Neosalvarsan and Neosilver Salvarsan. The solutions are made in freshly distilled water at room temperature, *i.e.*, 20–25° C. While some of the arsphenamines on the market require hot water for solution, it has been found that the original German Salvarsan and Salvarsan made in the United States according to the method of Ehrlich become much more toxic if dissolved in hot water. Furthermore, the latter are easily soluble in cold water. It is important that the Salvarsan be fully alkalinized so that the di-sodium salt is injected. This solution will have a slightly higher alkalinity than the blood. It is less toxic than either the solution of the hydrochloride or the solution of the mono-sodium salt of Salvarsan. Calibrated 1 cc syringes are used for making the injections.

At present the volume of solution prepared is 20 cc. *This is allowed to stand 15 minutes* before the first rat is injected. Three doses of the drug are injected in three rats each or in nine rats altogether. The doses are spaced at intervals of 20%, *e. g.*, 160, 200, and 240 mg. per Kg. for Salvarsan and that amount is considered the maximum tolerated dose which allows the survival of two out of three of the animals. Under the official regulations, 60% of at least 5 rats are required to tolerate 100 mg. per Kg. In the event that all die or all survive, it is necessary to decrease or increase the range of dosage to determine the maximum tolerated dose.

The second biological test on a product is that to determine its parasiticidal value. It is not practicable to determine this value directly upon the organism of syphilis, the *Treponema pallidum*, either in a test-tube or in the body of an animal. Fortunately, resort may be had to indirect methods which have been shown to be most valuable in estimating the relative value of an arsenical in the treatment of protozoal infections. Dale, in a series of experiments on Neosalvarsan, has shown that those preparations which are of high trypanocidal value in the laboratory are also, in general, most effective in clearing up the lesions of syphilis and eliminating the *Treponema pallidum* from the patients examined in his clinics; in other words, clinical results are paralleled in and may be predicted from the results of the experimental laboratory. Voegtlin, at the Hygienic Laboratory, has described a rapid and quite satisfactory method for the determination of the trypanicidal value of drugs of the Salvarsan type. The organism used is *Trypanosoma equiperdum*, the causative factor in a disease of horses known as "la dourine" or horse syphilis. It is non-infective towards man but is very virulent towards rats and mice, thus eliminating the possibility of spontaneous recovery of these animals. It is propagated by transferring a few drops of blood from an infected animal to the peritoneal cavity or blood stream of a fresh animal. In the absence of treatment the rat will certainly die in from three to five days after the appearance of organisms in the blood stream.

The test is conducted by inoculating a series of animals with the blood of a infected rat. The blood is so diluted that each animal receives from 50 million to 70 million living organisms. Each animal should show 100,000 to 250,000 organisms per cu. mm. twenty-four hours after inoculation. At present the tests at this laboratory are made by injecting three animals per dose and using three different doses at intervals of $33^1/_3$%. The animals which show 1,000 or less organisms per cu. mm. twenty-four hours after treatment are considered as

having received the minimum effective dose (M. E. D.) or over. That dose is the M. E. D. which is effective in reducing the organisms to 1,000 or less per cu. mm. in two of the three rats injected therewith.

It has been found that the virulence of the organism is subject to many variables and for this reason it is highly desirable to inject part of the rats on a given infection with a control preparation. By this means the accuracy and value of the method are considerably increased. For the past two years this laboratory has used a preparation of Salvarsan as a control.

It should be noted that the M. E. D. is not the dose which gives an absolute cure but is merely the dose which clears the blood stream of organisms for a short period. Voegtlin and Smith have shown it to be a function of the curative dose, therefore, it is permissible to use it as a means of measuring the relative parasiticidal value of different compounds and to assume that a product having a high M. E. D. as compared to the standard product (Salvarsan) will also have a relatively high curative effect in the treatment of disease. In using this method it is possible to get results in forty-eight hours after inoculating the animals with organisms whereas in the determination of the curative or sterilizing dose of earlier investigators at least sixty days' observation was necessary in order to be sure that no relapses would occur.

The method of injection of the drug in this test is that described for the toxicity test, using more dilute solutions since the M. E. D. is but a fraction of the tolerated dose. At present a uniform volume of 50 cc is used in order to allow a greater accuracy in weighing the drug.

Twenty-four hours after treatment a drop of blood is taken from the tail of each animal and a smear made. Those specimens showing organisms are noted and a count made to determine the number of parasites per cu. mm. This information is used to determine the M. E. D. as described above. The counts are made by diluting the blood with a carbol-fuchsin staining fluid and counting in the ordinary chamber used for counting blood cells.

Recent years have seen much progress in the application of quantitative methods to the biological testing of drugs. The improved methods of evaluating pharmaceutical arsenicals have had a two-fold aim in this laboratory: first, to give to the physician a Salvarsan and a Neosalvarsan of as low toxicity as is compatible with a high therapeutic activity thereby maintaining the most favorable chemotherapeutic ratio or index; second, to ascertain for the medical profession the toxicity and parasiticidal values of such new compounds as are synthesized by chemists for use in the treatment of disease.

COÖPERATION IN PHARMACEUTICAL RESEARCH.*

BY H. V. ARNY.

Two years since it was my privilege to present a paper before this association under the title "Research and the Cash Register" wherein it was pointed out that the publication of high grade research was of direct personal benefit to every mem-

* Read at the 53rd annual convention of the New Jersey Pharmaceutical Association, held at Spring Lake, June 12–15, 1923.

ber of the calling to which the research worker belonged. The paper was a plea for more interest in pharmaceutical research by all pharmacists; retail, wholesale or manufacturing. It urged encouragement of research by all pharmaceutical associations. It pointed out the desirability of research (especially along the line of problems in galenical pharmacy) by retail pharmacists. It revealed the hopes of some of us as to the development of agencies devoted to the proper recognition of pharmaceutical research.

During the two years that have elapsed since the reading of that paper gratifying progress has been made. The great research center of America, the National Research Council, now has a pharmaceutical sub-committee in its Division of Chemistry and a sub-committee on pharmaceutical botany in its Division on Biology and other points of connection with pharmacy are now being discussed.

THE NATIONAL CONFERENCE ON PHARMACEUTICAL RESEARCH.

While we must all admit that these affiliations of Pharmacy with the National Research Council are highly desirable there is need for a still closer coöperation, a clearing-house where all research workers in pharmacy may fore-gather for the interchange of views, for the giving and receiving of advice on research problems, for the devising of plans of coöperative research. This need was met by the organization last year of the National Conference on Pharmaceutical Research, which now includes among its members the following national associations.

American Conference of Pharmaceutical Faculties.
American Drug Manufacturers Association.
American Pharmaceutical Association.
Committee of Revision, United States Pharmacopœia.
National Association of Retail Druggists.

The following national bodies have expressed themselves as favoring affiliation in the Research Conference but have not yet become members.

American Chemical Society.
American Pharmaceutical Manufacturers Association.
Bureau of Chemistry, U. S. Department of Agriculture.
Committee on Revision, National Formulary.
National Association of Boards of Pharmacy.
Proprietary Association of America.

All six of these organizations will have delegates or "observers" at the second annual meeting of the Research Conference which will be held next September in Asheville.

A few words as to the research activities of the organizations just mentioned may be in order.

American Conference of Pharmaceutical Faculties, constituting the leading colleges of pharmacy in this country, is of course deeply interested in research. It has a Committee on Research, which has done good work in the past and has much more yet to do.

American Drug Manufacturers Association has a strong Scientific Section, which is doing magnificent work on unification of assay methods and on the study of monographs of the Pharmacopœia and of the Formulary. A visit to the sessions of the Section is an inspiration to any pharmacist fortunate enough to be present.

American Pharmaceutical Association, the mother of our national pharmaceutical organization, is the fountain head of American Pharmaceutical research. Not only are the most notable reports on research read at its annual meetings and published in its JOURNAL but research is also stimulated by the A. Ph. A. YEAR BOOK, by its Ebert Prize and by the annual grants now made from its Research Fund.

Committee of Revision, United States Pharmacopœia is a research agency without peer in this country. It is remarkable in the first place, as an organization that has been conducting research for over a hundred years. It is moreover one of the finest examples of practical coöperative research that the world possesses. Were its activities along lines other than medical and pharmaceutical, were it in the hands of people more expert along the lines of publicity, it would be known throughout the length and breadth of this land even as it is known to us pharmacists, as one of America's greatest scientific institutions.

National Association of Retail Druggists is more than an organization devoted to the commercial interest of retail pharmacy. Its leaders have ever felt the importance of research especially in the field of galenical pharmacy, as manifested in the valuable work of its Committee on U. S. P. and N. F. Propaganda.

The American Chemical Society, that great organization of 15,000 chemists of this country, includes in its membership practically every American pharmacist conducting research along chemical lines. These pharmaceutical chemists foregather at the sessions of the Division on Medicinal Chemicals held at the semi-annual conventions of the Society. A number of its non-pharmaceutical members are doing research that our own pharmaceutical group should be doing; thereby showing that research in pharmaceutical chemistry is of wide-spread importance and interest.

The American Pharmaceutical Manufacturers Association is doing work of great value to manufacturing pharmacy in the activities of its Committee on Formulas.

Bureau of Chemistry, U. S. Department of Agriculture, is not only known to us as the agency having on its hands the enforcement of the national food and drug law but also as an important factor in American research. Some of the finest research work along the lines of pharmaceutical chemistry and pharmaceutical botany is being conducted by the scientists of the Bureau.

Committee on Revision, National Formulary, like the U. S. P. Revision Committee, is doing coöperative research work of great value to American science in general and to American Pharmacy in particular.

National Association of Boards of Pharmacy is doing great work along the lines of pharmaceutical statistical research. In this line it occupies a unique field of service.

Proprietary Association of America has among its membership, firms whose chemists are doing noteworthy research work. The Association is also planning to have a research laboratory in the new Headquarters that it is building in Chicago.

The foregoing roll call of national organizations interested in pharmaceutical research covers rather fully but by no means exhausts the list of national organizations that should be affiliated with the National Conference on Pharmaceutical Research. The list however, justified the creation of the Research Conference and encourages the belief that with such support, the Research Conference will be able to accomplish much for American Pharmacy.

OBJECTS OF THE RESEARCH CONFERENCE.

Perhaps the question may be raised; what is the use of such a research conference?

There are so many things that the Research Conference can do, that it is impossible to relate all of its potentialities, but three or four items may suffice to show its need. In the first place there is a distinct need of an annual opportunity of getting together the workers in pharmaceutical research for an interchange of views.

Of course we have such a forum in the A. Ph. A. Scientific Section but that is a body designed to hear the results of research rather than to discuss research procedure. Then there are a number of chemists performing work along the lines of pharmaceutical chemistry, who do not attend the meetings of the American Pharmaceutical Association. It is hoped that in the Research Conference we can have all of these workers as delegates from the organization to which they give their primal allegiance.

Having gotten these research workers together, the next desirable aim is to plan coöperative research or what is of equal importance, to prevent duplication of research efforts. Taking a tangible illustration of each phase just suggested; here is a problem of pharmacopœial revision that needs solving. The dozen men constituting the U. S. P. subcommittee entrusted with the work on hand have enough to do with routine tasks and this particular problem requires expert handling. Of course, even now the expert in such work is sought out for advice, but if the Research Conference functions as it should, we will have a census of all workers in pharmaceutical research and know instantly who is the best man to consult on the special work on hand. On the other side, it has happened that after a member of the U. S. P. Revision Committee has worked as special referee on a certain topic, he finds the very work he has just done covered in a paper published just as the referee work is completed. If the census of pharmaceutical research workers includes work in contemplation as well as work already accomplished a good deal of lost effort will be eliminated.

A third aim will be the financial encouragement of pharmaceutical research. Of the millions that have been poured into research funds practically none has gone to pharmaceutical research. This statement may be challenged from one standpoint. Much money is going to pharmaceutical research or research that should be done by those trained in pharmacy but it is masqueraded under the names of medical research, chemical research or what not.

We pharmacists should have no objection to our friends in the sciences doing pharmaceutical research. It shows how great a field is open to the highly trained pharmacist. Nor have we the right to repine over the fact that money is going to pharmaceutical research under other names. It simply means that we pharmacists have not given sufficient publicity to the fact that there are many of us who are

capable, ready and anxious to do certain research work if only properly encouraged. A very important part of the work of the Research Conference will be to show what research work has been done in the past by trained pharmacists and how much more there is remaining to be done if only the proper financial encouragement is given.

Above it was stated that very little money is available for pharmaceutical research. The only considerable amount is in the American Pharmaceutical Research Fund, the available income from which affords grants now totalling $400 per annum. It seems more than likely that other national bodies when properly approached will make a provision for similar annual grants for pharmaceutical research; another specific illustration of the kind of work that can be performed by the Research Conference. However were I to enumerate all of the specific work which the Research Conference has before it, I would tire my auditors.

OTHER RESEARCH CONFERENCE AFFILIATIONS.

At this time the members of the New Jersey Association might ask; "What has all of this to do with us?"

In my previous paper I emphasized that all fine pharmaceutical research redounded to the credit of every member of our calling, but there is likely to be a more personal interest in the Research Conference by the members of the New Jersey Association in the near future.

Up to now the organizing efforts of the Research Conference have been directed solely toward national bodies but now that practically all available national bodies are lined up for the Conference, we are giving some thought to the affiliation of units other than national.

First there are all the colleges of pharmacy. These are now affiliated with the Research Conference through the national body the Conference of Faculties, but we all believe that a direct contact of the individual college and its research staff (which should mean its entire teaching staff) with the Research Conference is much to be desired. Then we have possible point of contact, giving promise of valuable results, between the Research Conference and the State pharmaceutical associations through their committees on papers and queries and similar scientific committees. As several of our State associations do not appear to have such scientific committees the proposition must be handled with State associations as individual organizations.

Nothing definite in this direction has been considered by the Research Conference, but it is likely that there will be created by the Research Conference an auxiliary committee consisting of the chairman of the committee on papers and queries or of a similar scientific committee of each State association having such a committee. Such a point of contact between the Research Conference and a State association would be of benefit to both, since each body would then have the opportunity of knowing what the other one was doing for research.

As just mentioned this is merely a possible activity of the Research Conference and I am not empowered to say anything more specific; but the topic is well worth our careful thought.

CONCLUSION.

In conclusion, I hope that I am leaving with you the impression that pharmaceutical research is well worth our sympathetic thought and that the National Conference is deserving of your confidence and support.

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THE BUSINESS SIDE OF PHARMACY

This department is devoted to the discussion of problems of business administration and commercial policies relating to the various branches of pharmacy.

CONDUCTED BY DR. ROBERT P. FISCHELIS.*

The editors of our pharmaceutical journals could render a real service if they would insist on the elimination of the word "ethical" from articles appearing in their publications when it is incorrectly used as a substitute for the words "professional" and "scientific." So often contributors to the pharmaceutical press and speakers at meetings of associations talk about *ethical* pharmacists and *ethical* pharmacy when the context of their papers or addresses clearly indicates that they either have no conception of that word or that they use it because they believe their readers or listeners know that they mean "professional" or "scientific," when they write or say "ethical."

The dual nature of the drug business of to-day makes it necessary to have some words or group of words to properly designate its divisions. This doubtless accounts for the introduction of the word "ethical," but its use in designating the professional or scientific side of pharmacy is unfortunate. Any business or profession which is conducted on an honest plane, and with due regard for the rights of the purchaser as well as the vendor, is an ethical business. A grocer, a hardware man, or a barber can be just as ethical as a physician or a pharmacist. Scientific knowledge does not affect a man's ethics or the ethics of a business. The moral standard which guides a business and the duty of the business man toward others in his own line and toward his clientele, constitute the ethics of that business or of the persons in it. The same is true of the professions.

It follows then that ethics has nothing whatever to do with the type of merchandise a man may sell or the service he may render in his drug store. When we look at the prescription pharmacy which specializes strictly on pharmaceutical work, it is not proper to say: "That is an ethical drug store," implying that the drug store at the next corner which has a soda fountain, a cigar stand, and sells a lot of miscellaneous merchandise, is not ethical. Both stores although totally different in the type of business on which they specialize are ethical pharmacies as long as they have a due regard for their obligations to society.

This question was forcibly discussed by Dean R. A. Lyman, at the recent convention of the New Jersey Pharmaceutical Association, when he pointed out that the drug store of modern times which gives a service to the public, both from a professional and business standpoint, is an institution of which pharmacy and the pharmacist need not be ashamed. It is only when such a business or its proprietor departs from the ethical standard that guides every decent business and profession to-day, that pharmacy is being harmed.

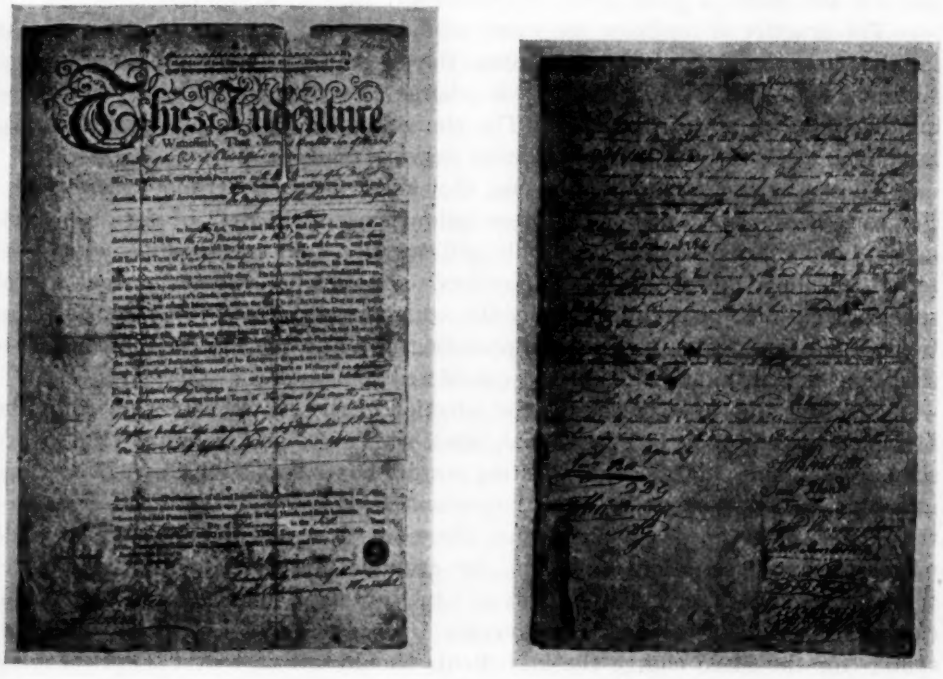
There is a growing feeling among students of pharmaceutical conditions that the present type of drug store has come to stay for a while at least and that the solution of our present problem is not a division of drug stores into two types. The professional work and the business work of the drug store can be carried on under the same roof, without any difficulty and certainly with much greater con-

* Dean, New Jersey College of Pharmacy.

venience to the public. It must be borne in mind, however, that the code of ethics which we have adopted covers both phases of the pharmacist's work.

When one reads the codes of ethics of various business men's organizations, such as the Rotary, Kiwanis and Lions Clubs, one gets a clear insight into the manner in which business men in general are striving to place commerce and trade on a higher plane. The old adage "caveat emptor" is no longer the maxim of business. Perhaps the fact that business men are striving to do things on a higher ethical basis is not wholly unselfish but it has had the effect of making it impossible for any organization to exist very long to-day which does not give either in goods or in service a dollar's worth for every dollar it receives.

In pharmacy, more so than in any other line of work, there lies an opportunity for leadership among business men in spreading the gospel of a greater service relation between those who buy and those who sell.



Left—Apothecary's Indenture, 1776, of Thomas Boulter, 9th apothecary of Pennsylvania Hospital, 1773. Right—Contract of Pennsylvania Hospital with Continental Army for Use of "Elaboratory," in 1778.—From "History Pennsylvania Hospital"—former, p. 480; latter, p. 62.

PRESCRIPTION PRICING.*

BY FRED W. AMES.

What shall I charge for this prescription? This is a question I have heard in my own and many other stores. Why that should be is more than I can understand.

* From a paper read before the Section on Commercial Interests, A. Ph. A., Cleveland meeting, 1922.

Prescription pricing, like prescription dispensing, is a science acquired by years of application and experience—knowing the cost of materials that enter the combination, comprehension of the value and knowledge of the time required in the compounding of the prescription, etc. There is no fixed rule; time required for dispensing can be figured to a nicety; prices of chemicals and pharmaceuticals fluctuate and, therefore, the cost should be calculated before pricing the prescription. The customer appreciates such care, he has assurance that there is no guesswork in pricing or compounding. Many pharmacists fix prices according to quantity without consideration of the cost or dosage—under such a plan the prescription which is supposed to yield a profit often constitutes a loss, and in the department where profit should bear a relation to professional service.

The prescription may be represented by a triangle—the patient, the physician and the pharmacist. The patient is the one benefited, and the one benefited always pays the price; incidentally, history has proved that the rich and well-to-do pay for the poor—a good point to remember.

The practice of medicine has more subdivisions to-day than ever before—the family physician or general practitioner, the surgeon, the specialist and the consultant; here we have four classes who charge according to different schedules—another good point to remember. The charges made by the pharmacist should have some relation to the professional service rendered.

The old pricing methods are wrong, they always were, never more than to-day. For convenience the work of the prescription department may be divided as follows: capsules, powders, cachets, pills, pill capsules, solutions for internal and external use, bulk powders, dusting powders, suppositories, ointments, and special surgical solutions. Narcotics require the same amount of work as other prescriptions, equal or greater care in compounding and the keeping of records. Prescriptions for alcoholics will not be considered.

The first step in dispensing is the selection of the container, representing the first cost—powder box, screw-cap vial, label, vials up to and including the 4-ounce size, up to 2-ounce ointment jar, dusting powder boxes, etc.—the cost will average, including breakage, about 10 cents; larger containers average from 15 to 25 cents—these costs bring no direct profit and, therefore, due allowance should be made when pricing prescriptions. Taking, for example, an ordinary 12 capsule prescription for which I charge $1.25 and up—the container costs 10 cents, the twelve capsules 5 cents, the ingredients average 15 cents—the gross profit will be 95 cents; for the $1.25 charge the ingredients should not cost over 25 cents. For powders I calculate along the same lines. For cachets I figure on from 15 to 25 cents each—25 cents when under six and 15 cents when twelve are ordered. The charge for ordinary combinations of pills in quantities of ten or under, 10 cents each; fifteen to twenty, 8 cents each; up to thirty, 6 cents each; up to fifty, 5 cents each; one hundred at 4 cents each. For pill capsules I make a flat extra charge of $1.00 per hundred in such quantities. For solutions for internal medication to be given in teaspoonful doses my charges are as follows: 1 ounce, 50–85 cents; 2 ounces, 85 cents to $1.25; 3 ounces, $1.25 to $1.65; 4 ounces, $1.35 to $2.00. 6 to 8 ounces, $1.50 to $2.50; pints $2.50 to $5.00. Solutions for external use average less, up to about $3.00 per pint, and special surgical solutions, with little medication, $2.00 per quart, and upwards.

Dusting powders are dispensed in sifting boxes, the minimum charge is $1.00. Careful dispensing of ointments requires considerable time and we charge for 1/2 ounce, 75 cents to $1.25; 1 ounce, $1.25 to $2.00; 3 and 4 ounces, $1.00 per ounce.

Narcotic prescriptions not less than $1.00; six capsules average $1.25, twelve capsules average $1.50 to $2.00; 1/8-grain hypodermic of morphine, $1.25 per tube; 1/4 grain, $1.50 per tube, etc. Lead and opium washes, usual strength, not less than $2.00 per pint.

My charge for suppositories is 50 cents each in quantities of half dozen or $5.00 per dozen. My suggestion to those who believe this to be an overcharge is that they time the work of the next prescription for suppositories.

Concentrations, drop dosage, bring prices governed, in a degree, by the patient —for saturated solution of potassium iodide, for example, we charge $1.25 per ounce, and 10 cents is added for a dropper. The prices for prescriptions for beautifiers, restorers and the like, are based on the intended purpose and the individual.

Patients who can or do afford medical service requiring specialists who exact large fees should be willing to pay for the best pharmaceutical service and, hence, my charges are not infrequently subject to conditions and not to fixed prices. Serums and other related products are dispensed at prices which afford a profit to me, making due allowance for money invested, frequency of sales, etc.

Prescription work requires not only skill and knowledge, but carries with it responsibilities—no reasonable charge can be too high, for the smallest error may seriously injure the business and a grave one is almost certain to destroy it—all of these considerations are to be taken into account with the stock and fixtures of the department and the expense of service connected with it. My advice to a druggist is—if he has not the courage to exact commensurate prices for prescription work—to discontinue the prescription department; there are other sales that can be made with profit without the responsibilities that obtain in the former. In my opinion the prescription department is comparable to the fire and police departments of a city, involving necessary expenses for the good of the community. Some say that it is personality which enables me to ask the higher prices, others that it is due to a wealthy clientele—I contend it is because my prices are just and right and the services are the very best that I am capable of rendering. Those who buy luxuries do not begrudge the prices paid; why should not the more important and necessary pharmaceutical service be adequately paid for? It will be—but the pharmacist must not lack in sincerity or assurance that his service is worth the price.

ADVERTISING NOT A COST FACTOR.

A recent editorial of the *New York Commercial* concludes:

"In almost every line of manufacture, the dominant factors are those who use advertising as business insurance and as the most economic method of gaining wide and steady distribution. A great many more business men would be using advertising to their advantage if they would clear their minds of the notion that it is not wise to use a certain percentage of the gross receipts of their business to advertise. On the contrary they should regard the matter of publicity as necessary and not as a superfluous cost. Inadequate advertising, badly prepared and placed in ineffectual mediums most certainly would represent not only cost but loss. There is just as much difference in properly conducted advertising and the haphazard kind as there is between careful manufacture and slip-shod production."

THE DEPARTMENT OF THE AMERICAN CONFERENCE OF PHARMACEUTICAL FACULTIES

[EDITOR'S NOTE.—In the symposium on "The Next Step" the editor takes the liberty of publishing a second letter from Dr. Edward H. Kraus of the University of Michigan, first because of an error in his original, and, second, because of the emphasis which he and many other men are placing upon the necessity of an educational survey of the Schools of Pharmacy. Furthermore, pharmaceutical educators throughout the country who know Doctor Kraus have read with much satisfaction of his acceptance of the deanship of the College of Pharmacy of the University of Michigan. His counsel will be welcomed by the Conference membership.

Resolutions adopted by the Michigan State Pharmaceutical Association, relating to a survey of pharmacy, are appended.

RUFUS A. LYMAN, *Chairman and Conference Editor.*]

THE NEXT STEP IN THE EDUCATIONAL PROGRAM OF THE AMERICAN CONFERENCE OF PHARMACEUTICAL FACULTIES.*

EDWARD H. KRAUS, University of Michigan: I was very much interested in the discussion which you conducted in the Department of the American Conference of Pharmaceutical Faculties in the May number of the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

I was pleased to note that the question of a survey of pharmacy by the Carnegie Foundation for the Advancement of Teaching is also considered by a number of other contributors as of fundamental importance at this time. I regret that the proofreader of this material failed to notice that a rather important part of the last sentence in my communication was omitted—the sentence reading: "In discussing the matter recently with a representative of the Foundation I was led to believe that conditions have changed somewhat more sympathetically in the past." This sentence, as it appears in my communication of March 7 to you, reads as follows: "In discussing the matter recently with a representative of the Foundation I was led to believe that conditions have changed somewhat *and that a renewed request would probably be received* more sympathetically than in the past." It is obvious that with the loss of the underscored line the sentence, as it appears, does not make good sense.

It is quite likely that our State Association which meets in Grand Rapids, June 12, 13 and 14 will adopt resolutions urging the Carnegie Foundation to undertake such a survey.[1] If other state associations have not taken action in this matter would it not be well to suggest it to their officers and to the pharmaceutical educators concerned? If the Foundation can be made to see that not only the educators but also that practicing pharmacists are vitally interested in this matter we may be able to get favorable action.

W. F. SUDRO, School of Pharmacy, Agricultural College, North Dakota: With reference to your requests as expressed in your letters of February 19th and March 10th as to the future educational program of the Conference, I am very pleased to submit the following suggestions.

The thought as expressed in your letter with reference to the three days a week school may be interpreted in an entirely different light than was actually the reason for the establishment of such an arrangement. Without doubt such an arrangement of courses was made for the distinct purpose of giving students the opportunity of assisting themselves financially while carrying on their educational program. In the educational plan as carried out at this school, it is distinctly impossible for any student to devote any particular amount of time to outside activities of this sort. Sometimes I wonder whether or not we are acting wisely in matters of this kind. You are well aware, of course, of the plan as adopted for some years by the College of Engineering of the University of Cincinnati, in requiring their students to devote a considerable length of time in practical work in the various factories. I know, of course, a very similar plan is in vogue at those institutions of pharmacy connected with large dispensaries, and I believe it is a step in the right direction. We do endeavor to place our students during the summer months

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* Continued from June issue, JOURNAL A. PH. A., p. 545.

[1] Resolutions have been adopted and are appended.

in as many pharmacies as possible, but in a great many instances we find that the druggists are not at all responsive to any such arrangement, particularly where a young man or woman has had no practical training to speak of.

The thought I had in mind was the fact that probably the three-day plan or a modification of it could very well be adopted in some form or other by the schools of the Conference. Such plan would not be at the volition of any student, but would be mandatory by the requirements of the school.

It will not be long now before all the schools of the Conference will be on a three-year basis, and possibly it may be well to think about what shall be done with that extra time. Would it not be a good plan for the Conference to go on record as demanding a minimum number of credits or units with reference to certain specified courses such as English, Mathematics, Political Economy, History, etc. I firmly believe that an expansion can be made with reference to many of our courses dealing with pharmacy, but I am of the opinion that if no well-defined program is meted out by the Conference, the extra time will be devoted chiefly to an expansion of pharmaceutical subjects. It has been my experience that students of our longer curricula are able to grasp the principles of pharmacy in a more thorough manner than those of our students who graduate from our two-year course.

I trust that the thoughts as advanced in the preceding paragraph may be found of some value to you in formulating future policies of the Conference.

WILBER J. TEETERS, University of Iowa: In my judgment, for the good of pharmacy in general, the following problems should be taken up by the American Conference of Pharmaceutical Faculties in the order in which I have given them, which seems to me to be the order of importance.

First—The standardization of the colleges. This would eliminate the incompetent institutions that are presuming to give what they are not. Full publicity to such a report of standardization would, in my judgment, do for pharmacy education what the Flexner report did for Medicine. As a result we would have fewer and better colleges of pharmacy and I predict that with such examination and standardization some of the colleges that now hold membership in the American Conference of Pharmaceutical Faculties would find it necessary either to very materially change the character of their institutions or, otherwise, they would find themselves among the eliminated number.

Second—The elimination of the three-day system of instruction now employed in some colleges. It is absurd to claim that students can get in three days what should be given in a six-day week.

Third—A system of grading of work done. The present system, or lack of system, should be eliminated and in its stead some system as near uniform as possible be adopted by all colleges of pharmacy.

C. C. BASS, School of Pharmacy, Tulane University: Through oversight your letter of May 1 was not answered more promptly, due, in part, to my absence from the city at the time of its arrival. Your letter, written in February, was also overlooked, for both of which I sincerely apologize.

In our own School of Pharmacy we are debating questions of importance of one kind or another. One of the important things is, no doubt, proper administration of admission requirements. I doubt whether our problems here are very different from those in other parts of the country. I feel, and I am sure the President of the University and the Board of Administrators also feel, that any extensive changes in the schools of pharmacy and education along these lines must be postponed until after some suitable agency shall make a proper survey of the schools of the country and the general needs, particularly the adoption by the licensing boards of the same requirements as now laid down by the schools of better grade.

One of the most helpful influences in education of any kind is the proper rating of the schools, so that the kind of work to be given at the different schools can be known by anyone who wishes to investigate. I believe that this is the great need—inspection and rating, with recommendations for improvement and classification of schools throughout the country.

JOHN J. MULLOWNEY, Medical College, Nashville, Tennessee: In reply to your letter of May 7th, I beg to say that it is my opinion that for the next three or four years you are asking about all that can be expected reasonably of the average candidate for a degree in pharmacy, when you ask them to train themselves for three years.

I heartily agree with you that every applicant for pharmacy should have four years of a high school course. Meharry has required this since about 1918. Possibly in three or four years it would be well to require four years for a degree in pharmacy, but for the present, I am of the opinion that three years on top of a good high school course is about all the public and the candidate can do.

J. A. KOCH, University of Pittsburgh: The next step in our Conference program I think will be to bring about the general recognition and adoption of the three-year course. While this course has been adopted by the Conference, I think that the majority of the colleges holding membership feel that the adoption is not at all fixed or binding. I believe that the three-year course will be quite generally adopted all over the country in 1925, but feel that it will be necessary for us to do quite a little diplomatic missionary work to bring this about.

MARIANO V. DEL ROSARIO, The University of the Philippines: I have received your favor of February 19th when our college year was ending and I regret the delay of this answer due to the fact that examinations, commencement, etc., came at the same time.

Referring to your question as to the next step which the Conference colleges and schools must have in prospect, I should say that it is the adoption of the compulsory four-year course in pharmacy leading to the unique degree of Bachelor of Science in Pharmacy.

In the Philippine Islands, it was already agreed upon by the faculties of the five schools and colleges and the board of pharmacy to raise our three-year course to a four-year course, and through the action of the Philippine Legislature I am fully confident that our freshmen of 1924 will have it.

The condition of the pharmaceutical profession in this country is far different from those in the United States. Among all the drug stores in the islands, which may be less than one thousand, there are only six or seven established in the American fashion with soda fountain and other sundry articles absolutely strange to the profession. Most of the rest, I may state, are conducted in the European style and our school is the one to lead our graduates in a new direction. As you can see in our new curriculum, a copy of which will be forwarded to you, our aim is to prepare the pharmaceutical chemist to be a true help to the physician, and in addition to his drug store maintain a laboratory in a way similar to the French pharmacies.

This measure is extremely beneficial and suits our local conditions mainly in provinces where the few practitioners have not time to devote to this kind of examinations.

So far, two of our graduates are working as junior bacteriologists in the Bureau of Science of the Government and some others are thinking to open their private laboratories.

In connection with your request of sending you something for publication I may inform you that I have just forwarded to Mr. Maronon an address which I delivered in the last Philippine Pharmaceutical Convention. I suppose you remember Mr. Maronon who represented our school in the last meeting of the American Conference. He may inquire if the paper can be published in the JOURNAL for it contains also some remarks about the profession.

RESOLUTIONS ADOPTED BY THE MICHIGAN STATE PHARMACEUTICAL ASSOCIATION, GRAND RAPIDS, JUNE 13, 1923.

Inasmuch as the action of the President and Board of Regents of the University of Michigan in appointing Dr. Edward H. Kraus, Dean of the College of Pharmacy, meets with the most hearty approval of the pharmacists of the state, be it:

Resolved, that the Michigan State Pharmaceutical Association in convention assembled in Grand Rapids, June 13th, 1923, place itself on record as commending this action on the part of the University authorities, and be it further

Resolved, that copies of this resolution be mailed to the President of the University of Michigan, and to the members of the Board of Regents.

To Dean Edward H. Kraus:

Realizing the importance which your services will mean to Pharmacy, both state and national, and understanding that you have accepted the Deanship of the College of Pharmacy of the University regardless of your other University activities, we, the members of the Michigan State Pharmaceutical Association, wish to express our hearty appreciation of your decision in accepting this appointment.

RESOLUTIONS ADOPTED BY MICHIGAN STATE PHARMACEUTICAL ASSOCIATION RELATIVE TO A SURVEY OF PHARMACY.

WHEREAS, Very great progress has been made in the last quarter of a century in all sciences, especially in those upon which the health of the public depends, and

WHEREAS, The pharmacist by training and association with the members of the Medical and Dental professions is most vitally concerned with all such advances and movements, and

WHEREAS, In the mind of the general public the status of the pharmacist to-day is not as important and as dignified as formerly, although his responsibilities to the State and the Nation are constantly becoming greater through legislative action, and

WHEREAS, The general trend in this country is toward higher educational requirements for all professions, such advanced standards being already effective in the allied sciences of Medicine and Dentistry, and

WHEREAS, Various States and Colleges of Pharmacy have already adopted such increased educational requirements, while other States and Colleges of Pharmacy apparently are content with existing standards, which condition is causing much confusion, and

WHEREAS, In our opinion legal and educational requirements should be more nearly uniform throughout the country, which result can be best accomplished by the adoption of standard requirements for licensure and for admission to and graduation from Colleges of Pharmacy, and

WHEREAS, The Carnegie Foundation for the Advancement of Teaching, through its searching and constructive studies on Medical Education in this country, Canada and Europe, contributed greatly to the present improved condition of Medicine and Medical Education, and

WHEREAS, A similar study of Dentistry and Dental Education is now in progress and nearing completion, and

WHEREAS, The American Conference of Pharmaceutical Faculties has, on several occasions, requested the Carnegie Foundation to undertake a similar study of the present status of Pharmacy and Pharmaceutical Education in this country;

Be It Therefore Resolved, That we, the members of the Michigan State Pharmaceutical Association, assembled in annual convention in Grand Rapids, June 13th, 1923, most heartily approve of the action of the American Conference of Pharmaceutical Faculties in this matter, and

Be It Further Resolved, That we most earnestly urge the Carnegie Foundation for the Advancement of Teaching to undertake the suggested study of Pharmacy and Pharmaceutical Education in this country, believing that of all the organizations in this country the Foundation is the best qualified to undertake such a searching and critical study in view of its experience and splendid results in the allied professions of Medicine and Dentistry, and

Be It Further Resolved, That copies of these resolutions be sent to the President of the Carnegie Foundation for the Advancement of Teaching, to the President of the University of Michigan, to the members of the State Board of Pharmacy, and to the various Pharmaceutical Journals.

PROCEEDINGS OF THE LOCAL BRANCHES

"All papers presented to the Association and its branches shall become the property of the Association, with the understanding that they are not to be published in any other publication than those of the Association, except by consent of the Committee on Publication."—By-Laws, Chapter X, Art. III.

Reports of the meetings of the Local Branches should be mailed to the Editor on the day following the meeting, if possible. Minutes should be typewritten, with wide spaces between the lines. Care should be taken to give proper names correctly, and manuscript should be signed by the reporter. To maintain its activity and representation each branch should see that at least three of its meetings during the year are reported in the JOURNAL.

INDIANAPOLIS.

The May Meeting of the Indianapolis Branch, A. Ph. A., was held at the Indianapolis College of Pharmacy, May 7th. An invitation was extended by the faculty in order to interest the students in the work of the American Pharmaceutical Association and quite a number of the students were in the audience.

The first number on the program was by Prof. E. H. Niles, Dean of the College, who had for his subject, "Medicinal Value of Some Foods Classed as Medicines." Professor Niles discussed the whole list of "Medicines" which have been recognized by the U. S. P., since its first issue in 1820 up to the present time, and which are usually considered foods.

If, however, they were foods pure and simple without any medicinal value they would not have been recognized by the U. S. P., and while some have been dropped in the various revisions, many still remain in the present edition on account of their medicinal value.

The difference between Orange Juice which is laxative and Pineapple Juice which is astringent, while both are acid and thirst quenchers, was explained.

Raisins, prunes and figs are considered for their laxative properties while oatmeal, barley, tapioca and sago are valued as demulcents, and while all of these are valuable foods yet their medicinal value exceeds their food value.

Arrowroot, wheat starch, potato starch and corn starch deserve recognition for their mechanical help in many processes, but they are also useful as antidotes, notably Iodine poisoning.

Sugar, molasses, glucose and honey are used as preservatives and mediums for administration of many remedies, also lard, suet and tallow as vehicles for medication, while elderberry, salt, pepper, mustard, vinegar and olive oil are used strictly for their medicinal value and chemical effects.

There is no abrupt line of distinction between—when a food is a medicine or when a medicine is a food.

After some discussion, which brought out many interesting facts which many had overlooked, the second number was presented by S. A. Cain, Professor of Botany at the Indianapolis College of Pharmacy, who had for his subject, "The Present Status of Vitamins." He stated that in spite of the fact that the knowledge of Vitamins is practically only ten years old the word has become an integral part of our vocabularies as well as of our diets. Yet it is a matter of fact that Vitamins are not fully understood even by those who are working with them.

The idea which was prevalent that for complete nutrition of an animal organism only proteins, fats, carbohydrates, salt and water were necessary has been broadened to include additional dietary components necessary to life, spoken of as Vitamins.

According to Funk (1922) the classification is as follows: A. for Antirachitic; B. for Antiberiberic; C. for Antiscorbutic. The first usually called fat-soluble, the other two water-soluble. Funk disproves this, claiming it "logically and chemically" incorrect, and his view is generally accepted. On the other hand Funk's spelling *Vit-amine* has generally been changed by dropping the final "E" and with it the "amine" significance that they are nitrogenous.

According to Hess, McCollum and others "A" has been recognized as curative for both rickets and xerophthalmia and neither A nor B are considered entities but include other types.

C. H. Hunt calls the antirachitic Vitamin "D" and reserves "A" for that portion which has other properties.

Funk and Dubin corroborated Emmett and Luros in their statement that yeast is

not identical with "B" but also contains "D," which would indicate that there are two "D's" claimed at present, one from "A" the other from "B," the properties of one differing from the other.

Mr. Cain then spoke at length on the importance of Vitamins and the nature of each, explaining each food article as to their Vitamin content and preservation of these in the method of preparing the food.

He spoke of the source of Vitamins in the higher plants and their power to synthesize these in the growing parts of the plant and process of storing. He also gave some interesting facts concerning the effect of Vitamins on various Bacteria.

The discussion following the address brought out many interesting points.

The Secretary then read a list of new members.

Ernst Stahlhuth, *Secretary.*

NORTHWESTERN.

The Northwestern Branch, A. Ph. A., held a meeting June 8. The Branch met jointly with the Wulling Club, which is made up of the entire student body of the College of Pharmacy. The reading of the last minutes was dispensed with. Dean Wulling spoke briefly on the value of membership in the A. Ph. A. and other associations. Dr. C. H. Rogers gave a ten-minute address on "Recent Advancements in Pharmaceutical Chemistry." Chairman Huhn gave a twenty-five minute address on "Advancing Standards of Ethical Pharmacy." Dr. Newcomb followed with an interesting paper on "Sources of Medicinal Plants and Seeds." The paper was prepared in reply to the many inquiries that have been received by the College of Pharmacy, University of Minnesota, concerning the procuring of medicinal seeds.

The hour for adjournment having been reached, a paper by Dr. Bachman on "Some Observations on Emulsion-Making" and a paper by Dean Wulling on "Cultivation of Medicinal Plants by Individual Pharmacists," were read by title.

The meeting was a spirited and animated one and proved profitable to all who attended

COUNCIL BUSINESS

CONSTITUTION OF THE AMERICAN PHARMACEUTICAL ASSOCIATION—PROPOSAL TO ALTER.

In order to meet any contingency which may arise in connection with making effective the present plan of reorganization of the Association, it is proposed to change Article III of the Constitution to read as follows:

"The officers of the Association shall be a President, three or more Vice-Presidents, a Secretary and a Treasurer, all of whom shall be elected annually. They shall hold office until the installation of their successors."

Signed:
E. F. KELLY,
A. G. DUMEZ.

A. PH. A. COUNCIL LETTER NO. 12. (Abstract.)

Washington, D. C., May 17, 1923.

To the Members of the Council:

62. Motion to appropriate $150 to purchase a mimeograph for the Secretary of the Council.—Carried.

63. Election of active members (Item 61). Applicants Nos. 274–311 elected to active membership.

64. Final action of the Division of Biology and Agriculture of the National Research Council with reference to the Committee on Pharmacognosy and Pharmaceutical Botany. (See Items 21, 32, 53 and 56.) The action taken with reference to this Committee is fully stated in the following letter:—

"May 8, 1923.

Dr. H. W. Youngken,
Philadelphia, Pa.

Dear Dr. Youngken:

I am pleased to inform you that the Division of Biology and Agriculture approved the recommendation to change the status of the present Committee on Coöperation from the American Pharmaceutical Association to that of a Committee on Pharmacognosy and Pharmaceutical Botany of the Division.

In this connection I wish to call your attention to the policy within the Division, that in the case of Divisional committees the Division appoint the chairman with the understanding that the balance of the committee shall be selected in conference between the committee chairman and the Division chairman, subject to the approval of the Executive Committee of the Division. However, the action of the Division in changing the status of the Committee on Coöperation carries with it the understanding that the personnel of the Committee on Pharmacognosy and Pharmaceutical Botany be the same as that of the present Committee on Coöperation from the American Pharmaceutical Association, and that it function with its personnel for the next fiscal year, that is to say, until June 30, 1924, at which time I should say the general policy of the Division quoted above will apply.

I trust that now the way is prepared for the active development on a high plane of the research interests in the field of Pharmacognosy and Pharmaceutical Botany. I may at this time state that the next meeting of the Executive Committee of the Division will be held some time during next July. Should you in the meantime wish to present any matters, I am sure the Committee would be glad to give them consideration at that time.

I am sending copies of this letter to Dr. Arny and Dr. DuMez. I am also notifying the other members of the committee of the action by the Division.

Very sincerely yours,

J. R. SCHRAMM, *Executive Secretary*, Division of Biol. & Agric., Nat'l Research Council."

65. Acknowledgment of receipt of Proceedings and Year Books by the Pharmaceutical Institute of the University of Dorpat. Under date of April 6, 1923, Prof. Stamm writes as follows:

"American Pharmaceutical Association.

Gentlemen:

Your letter of 10th of March, as also the box with the books, I have just received from the university library. The box contained the following books which are inscribed in the institut biblioteka sub. Nos. 15 and 16:

1. No. 15: *Proceedings of the American Pharmaceutical Association*, Vol. 1858, 1860, 1862–1888, 1891–1911 and Index 1851–1902.

2. No. 16: *Year Book of the American Pharmaceutical Association*, Vol. 1912–1920 (1–9).

Very thankful for the great present and all the trouble you have seen for us,

I am very respectfully,

Prof. J. STAMM, *Director*."

66. Election of active members: No. 312, Arthur Hofmann, 382 Cornelia St., Brooklyn, N. Y.; No. 313, Henry David McNierney, 480 E. 183 St., New York; No. 314, Albert Robert Caua, 373 Manhattan Ave., Brooklyn, N. Y.; No. 315, Edward A. Strauss, Fordham Univ. Coll. of Phar., New York, N. Y.; No. 316, Jeremiah Francis LaPorte, 2245 Second Ave., Man., N. Y.; No. 317, Henry Herbert Schumann, 2636 University Ave., New York City; No. 318, Henry S. Goldey, 525 A. Humboldt St., Brooklyn, N. Y.; No. 319, Peter Albert Schroeder, 654 Grace St., Chicago, Illinois; No. 320, Standlee Irving Twitchell, 1646 W. Congress St., Chicago, Ill.; No. 321, Michael Glickman, 2448 W. North Ave., Chicago, Ill.; No. 322, Clifford Hoaglund, 137 W. North Ave., Chicago, Ill.; No. 323, Cornelia Cunningham, U. S. Veterans' Bureau, Knoxville, Tenn.; No. 324, Louis Weiner, 1335 Penn Ave., Pittsburgh, Pa.; No. 325, Jennie Kroopuick, 226 N. Gilmor St., Baltimore, Md.; No. 326, J. J. Possehl, 1102 Wells St., Milwaukee, Wisconsin; No. 327, Emil Wepfer, Neillsville, Wisc.; No. 328, Fred E. Welmer, 1546 S. New Jersey, Indianapolis, Ind.; No. 329, Newton William Reid, 406 S. Butler, Indianapolis, Ind.; No. 330, Romulus Augustus Hedgpeth, 1001 E. Marshall St., Richmond, Va.; No. 331, Warren H. Martin, 210 S. 3rd St., Richmond, Va.; No. 332, Josiah William Chambler, 206 W. Grace St., Richmond, Va.; No. 333, Harlan J. Mentzer, Blue Ridge Summit, Pa.; No. 334, Albert A. Branch, 206 E. Franklin St., Apt. 6, Richmond, Va. (after June 1st, Ettrick, Va.); No. 335, Emma W. White, 318 N. 6th St., Hopewell, Va.; No. 336, Myrtis McKinley Jennings, Elk Hill Va.; No. 337, Harvey R. Haag, 1628 Beverly St., Richmond, Va.; No. 338, Austin Rowe Lawrence, Alderson, W. Va.; No. 339, S. B. Groisser, 426 Ralph Ave., Brooklyn, N. Y.; No. 340, John Scavo, 235 Alexander Ave., New York, N. Y.; No. 341, Russell R. Williams, 1713 Mt. Vernon St., Philadelphia, Pa.; No. 342, Herald D. Keiser, 201 S. Front St., Milton, Pa.; No. 343, Bernard Theodore Laskowski, 2714 East Lehigh Ave., Phila., Pa.; No. 344, George Henry Heckman, 39 Mauch Chunk

St., Nazareth, Pa.; No. 345, Herman Frank Winger, 230 Adrain St., Emaus, Pa.; No. 346, Paul F. Himmelberger, 639 Penn St., West Reading, Pa.; No. 347, Aaron Lichtin, 1545 S. 7th St., Philadelphia, Pa.; No. 348, William A. Kelley, 1809 N. Camac St., Philadelphia, Pa.; No. 349, Albert H. Fubler, 404 Columbus Ave., Boston, Mass.; No. 350, Orville Pierce Watson, 2600 Yonge St., Toronto, Ont., Canada.

A. G. DuMez, *Secretary.*

A. PH. A. COUNCIL LETTER NO. 13.

WASHINGTON, D. C., JUNE 11, 1923.

(Abstract.)

To the Members of the Council:

67. Applicants Nos. 312 to 350 elected to active membership.

68. (Motion No. 23.) *Selection of convention headquarters.* It is moved by J. G. Beard, seconded by A. G. DuMez, that Kenilworth Inn, Asheville, N. C., be selected as the official headquarters for the seventy-first annual convention.

This motion has the endorsement of the local committee on entertainment.

69. University of North Carolina Branch elects a Council Representative. Under date of May 18, 1923, Secretary Westbrook of the Univ. of North Carolina Branch writes from Chapel Hill as follows:

> "This is to inform you that at the last regular meeting of The University of North Carolina Branch of the American Pharmaceutical Association Dean E. V. Howell was elected as Member of the Council to represent this branch in the Council.
>
> Perhaps you will be interested to learn that since the charter was granted the membership of the branch has been increased to sixty-four members."

70. Report of committee to audit the Treasurer's accounts. The following report of the committee appointed by the Chairman of the Council to audit the accounts of the Treasurer was received June 9, 1923:

> "In accordance with the instructions received from Mr. Samuel L. Hilton, Chairman of the Council, we the undersigned Committee beg to submit the following report:
>
> We have examined the books of the Treasurer of the American Pharmaceutical Association, and we find that his report for the year Jan. 1, 1922 to Dec. 31, 1922 has been audited by Mr. W. Albert Johnson, a certified Public Accountant, who has submitted a statement of the financial transactions of the Association, same having been found correct.
>
> As far as possible, we have checked the balances on deposit in the different banks and find same in accord with the books of deposit.
>
> We have also verified the Securities, having counted the bonds, which are stored in the safe deposit box at the National Exchange Bank, Baltimore, and find same to be in accord with the records.
>
> The books are kept in a neat and careful manner and we wish to commend the Treasurer for his efficient work."
>
> Respectfully submitted,
>
> JNO. O. MUTH,
> CHAS. L. MEYER,
> CHAS. C. NEAL,
> *Committee.*

71. (*Motion No. 24.*) *Motion to supply the University of Strasbourg with certain back numbers of the Journal.* In response to the request which follows it is moved by Secretary Day, seconded by President Koch, that the Editor send to the Library of the University of Strasbourg the back numbers of the journals needed to complete the set, in so far as he is able to supply them from his stock.

> University and Regional Library
> 6 Place de la Republique,
> Strasbourg, 21 April, 1923.
>
> Mr. President of the
> American Pharm. Assoc.
>
> I have the honour to bring to your notice the fact that since 1915 we have received no copies of the Journal of the A. Ph. A., which previous to that date you were kind enough to donate to us.
>
> I am taking recourse, therefore, in your good will in asking if it would be possible for you to supply the University and Regional Library of Strasbourg with the volumes which we do not now possess, to wit: Vol. IV (1915), Nos. 8–12; Vol. V (1916) and those following.
>
> I beg you to accept, sir, the expression of my high regard.
>
> The Administrator of the University and Regional Library.

72. (*Motion No. 25.*) *Election of active members:* No. 351, Carl Laubscher, c/o U. S. Marine Hospital No. 19, 14th Ave. & Lake Street, San Francisco, Calif.; No. 352, Forest J. Goodrich, 1403 East 56th Street, Seattle, Wash.; No. 353, Martin H. Smith, 150 Lafayette St., New York City, N. Y.; No. 354, Asbury Osman Leonard, No. 70 Fifth Ave., New York City, N. Y.; No. 355, John Thomas Connally, 1410 St. Mary St., Beeville, Texas; No. 356, Joseph Raphael Betuska, 34 Winthrop St., Holliston, Mass.; No. 357, S. P. Dutton, Meadow View, Va.; No. 358, Sister M. Bernadette Hogan, 720 S. Brook St., Madison, Wis.; No. 359, Peter Alexander Di Monaco, 19 Henchman St., Boston 16, Mass.; No. 360, Hermon McDonald, 653 Garfield St., Valparaiso, Ind.; No. 361, Leroy W. Stahler, 77 Erskine St., Detroit, Mich.; No. 362, Ralph Blauer, Osborne, Kansas; No. 363, J. Floyd McMullin, 73 So. 12th St., Kansas City, Kansas; No. 364, Alf Raymond Ahlstrom, 428 Madison St., Topeka, Kansas; No. 365, Clarence E. Schrepel, 2505 E. 37th Street, Kansas City, Mo.; No. 366, Walter W. Hammond, 831 N. Euclid Ave., Pittsburgh, Pa.; No. 367, Glenn H. Bowyer, 942 Neville Ave., Follansbee, W. Va.; No. 368, Arthur Earl Warstler, 134 Brighton St., Rochester, Pa.; No. 369, Merritt Campbell Schultz, 538 Park Ave., Johnstown, Pa.; No. 370, Edward I. Labowitz, 6 Freeport St., Etna, Pa.; No. 371, Thomas J. Janda, Jr., 1017 E. Ohio St., Pittsburgh, Pa.; No. 372, Carl Alexander Wirts, 3738 Perrysville Ave., Pittsburgh, Pa.; No. 373, George C. Stamm, 408 Kingsboro St., Pittsburgh, Pa.; No. 374, Floyd Benton Souders, 101 Hay St., Fayetteville, N. C.; No. 375, Vincent J. Kucenicz, 1203 Glenn St., Homestead, Pa.; No. 376, Howard Golburn Powley, 1015 Highland Place, Altoona, Pa.; No. 377, Samuel Storch, 386 Hinsdale St., Brooklyn, N. Y.; No. 378, Henry Nielsen Bexfield, 1416 South 17th Ave., Maywood, Ill.; No. 379, Isidor B. Facton, 283 Wallabout St., Brooklyn, N. Y.; No. 380, Burrel Theodore Williams, Chapel Hill, N. C.; No. 381, Joseph Claxton Harris, Chapel Hill, N. C.; No. 382, Jones Douglas Bain, Chapel Hill, N. C.; No. 383, Roy Archibald Moose, Chapel Hill, N. C.; No. 384, Maynard Dennis West, Chapel Hill, N. C.; No. 385, Wesley Jones Hickman, Chapel Hill, N. C.; No. 386, Charles Henry McDonald, Chapel Hill, N. C.; No. 387, Henry Clay Ross, Chapel Hill, N. C.; No. 388, Franklin Troy Mitchell, Chapel Hill, N. C.; No. 389, William Russell McDonald, Jr., Chapel Hill, N. C.; No. 390, Graham Page Johnson, Chapel Hill, N. C.; No. 391, Edward Rogers Goodyear, Chapel Hill, N. C.; No. 392, Waits Artemus Ward, Chapel Hill, N. C.; No. 393, Fred Henry Flemming, Chapel Hill, N. C.; No. 394, Alonzo L. Gilreath, Chapel Hill, N. C.; No. 395, Frank B. Kendall, 503 N. Osage St., Girard, Kansas; No. 396, W. A. Thaw, Conway Springs, Kansas; No. 397, Valentine C. Bartlett, 224–230 West Huron St., c/o The Orangeine Chemical Co., Chicago, Ill.; No. 398, Roy P. Taylor, c/o Ash Drug Store, 611 N. Broadway, Pittsburg, Kansas; No. 399, Eugene Russo, 1531 Beechview Ave., S. Hills, Pittsburgh, Pa.; No. 400, Sam J. Kelly, Olathe, Kansas; No. 401, A. P. Cloud, Jena, La.; No. 402, Raymond Paul Markel, 356 E. 59th St., Chicago, Ill.; No. 403, Maurice Radner, 1443 S. Trumbull Ave., Chicago, Ill.; No. 404, Bernard Franklin Harris, 1440 N. Leavitt St., Chicago, Ill.; No. 405, Leonard E. McHugh, 410 S. Clinton St., Iowa City, Iowa; No. 406, Virgil Paul Shaefer, 814 Sixth Ave., Altoona, Pa.; No. 407, Sidney Stone, 1800 So. Homan Ave., Chicago, Ill.; No. 408, Harold Goldstein, 5544 Wilkins Ave., Pittsburgh, Pa.; No. 409, William Davis, 1545 Wylie Ave., Pittsburgh, Pa.; No. 410, Jacob Louis Cohen, 360 Ophelia St., Pittsburgh, Pa.; No. 411, Joseph Cianciarulo, 190 Maverick St., East Preston, Mass.; No. 412, Benjamin Harrison Quarles, 339 Summit St., Mt. Oliver P. O. Pittsburgh, Pa.; No. 413, Wm. Ralston Lecky, Jr., 2220 Stuart Ave., Richmond, Va.; No. 414, William James Kearney, 112 Curry Street, Phoebus, Va.; No. 415, Miss Sarepta Meade Hodges, 548 Main St., Danville, Va.; No. 416, William Randolph Burgoyne, 108 South Third St., Steubenville, Ohio; No. 417, Robert Inglis Beddoe, 1005 15th Street, Bedford, Ind.

A. G. DuMez, *Secretary.*

EDITORIAL NOTES

Editor: E. G. EBERLE, Bourse Building, Philadelphia, Pa.

Committee on Publication: A. G. DUMEZ, *Chairman;* S. L. HILTON, H. M. WHELPLEY, R. A. LYMAN, W. L. SCOVILLE, and the Editor-in-Chief of the JOURNAL, General Secretary, Treasurer and Reporter on the Progress of Pharmacy, *ex-officio.*

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PROPOSAL TO ALTER CONSTITUTION OF AMERICAN PHARMACEUTICAL ASSOCIATION.

Members of the American Pharmaceutical Association are directed to the proposal to amend the Constitution of A. Ph. A. Formal notice is given under Council Business of this issue of the JOURNAL, in comformity with Article V of the Constitution—see p. xxvii in YEAR BOOK, Vol. 10.

ERROR IN A FOOTNOTE REFERENCE RELATING TO "CALIFORNIA BEES."

Dr. A. B. Lyons has called attention to errors in page numbers in a footnote on p. 939 of Volume X, JOURNAL A. PH. A. The page numbers should be 510 and 1111 instead of pp. 570 and 571. The suggestion is made that the numbers be corrected accordingly.

CLAIMS INCREASE OF DIABETIC CASES DUE TO LARGER CONSUMPTION OF SUGAR.

Dr. Benjamin Jablons in the course of a lecture at St. Mark's Hospital, New York, made the assertion that prohibition has been the indirect cause through the substitution of sugars and fats to produce the heat formerly furnished by alcohol of doubling the number of diabetes cases in this country.

THE CAMERA IN DIAGNOSING DISEASE.

In an address before the Broome County Academy of Medicine, May 29, Dr. Alfred B. Hitchins declared each disease has a specific photo reaction which, if properly studied, will identify the ailment from which a patient is suffering. The new method will be valuable in identifying disease through the chemistry of the blood and will open up a new field of physical diagnosis, Doctor Hitchins declared.

A CONSULTATION WITH M. GRUBY.

William H. Gano has translated for the JOURNAL A. PH. A. portions of an article from *The Journal of the Pharmaceutical Historical Society*, Paris, of January 1923. The contribution is by Dr. Henri Leclerc and the subject relates to M. Gruby who was for many years "a specialist" in the treatment of neurasthenia, etc. His prescriptions were of harmless composition; observance of dosage, time and methods contributed chiefly to the success in restoring the patients. The prescriptions will be omitted at this time, but a few anecdotes which Dr. Leclerc reported are presented; these will go to prove that M. Gruby was not, as has been said, a vulgar charlatan, but a keen observer, a true philosopher, who believed that "where skill is unsuccessful, audacity is often useful." The following will show to what extent he knew the psychology of the sick. Thanks to the mystery with which he surrounded himself and to the allurements of a mystic healer, beneath which he hid real science, he drew the blind confidence of many intellectuals of Paris—his patients were mostly neurasthenics and nerve-jaded. In submitting them to his bizarre and complicated treatment, he attacked the mind and turned their attention from ills which were frequently imaginary; often obtaining results which had been vainly sought for through the use of classic therapeutics. Some of his prescriptions might easily be taxed with charlatanism although they proved to be truly God-sends, showing a profound knowledge of human mentality.

Gruby was consulted by Alexander Dumas, the writer believing himself a victim of a grave stomach malady. He was ordered a régime of hard boiled eggs, beef boiled with salad—the whole to be washed down with copious

draughts of red wine. Some time after, Dumas returned for another consultation—"Well," said Gruby, "how are you?"—"Not any worse, not any better," replied Dumas. "What," exclaimed Gruby, "not any worse and on such a régime, and you tell me you have stomach trouble? Ridiculous!"

A lady, victim of an intense imaginary malady, consulted him one day. "The case is serious, very serious," said Gruby, "it requires energetic treatment; you must take each day, a glass of wine between two glasses of water; above all things make no mistake, it would be terrible." The lady inverted the order of the factors, she took the wine first, then the water—badly frightened and fearing a catastrophe she rushed to Gruby. "The situation is grave," said he, "but it can be saved, you must immediately take a glass of water—then the wine will be between the two waters.

To another patient he prescribed the purchase of an orange at a certain grocer's, some distance away—and to eat half of it in walking up the Champs-Elysées—the other half to be eaten in returning.

A lady, now an octogenarian, and a patient of Dr. Leclerc, relates the following: "Living in comfort and idleness—with no other occupation than the accomplishment of social duties, calls, the play, and dinners—she presented the characteristic symptoms of the beginning of arteriosclerosis (obesity, panting, headache, vertigo); not wishing to change her manner of living, she tried a host of remedies without benefit; finally, she consulted Gruby, who advised her to live 15 days each month on salads, with cream cheese and gingerbread for breakfast; a light cake soaked in an infusion of dried almond shells for lunch, and for dinner a soup made of salsify. Besides, every morning at 9 o'clock she was ordered to go on foot to a certain herborist of L'Ile Saint Louis, and procure a package containing 5 Gm. of wild pansy with which to prepare an infusion to be taken at 8:30 in the evening, *at the moment of retiring*. The patient, a woman of intelligence, soon grasped the idea, hidden beneath these directions—that her affliction was more amenable to exercise and a wise diet than to polypharmacy."

INSULIN.

A comprehensive article in the *Journal of the American Medical Association*, of April 28, pp. 1238–1241, concludes with the following statement: "It appears, then, that as a result of a vast amount of research on diabetes mellitus, and still earlier on the physiology and pathology of the pancreas, researches by numerous investigators all over the world, conducted largely on experimental animals, as well as with human beings, there has finally been evolved from the pancreas a principle which has a specific effect on the carbohydrate metabolism of the body. The effects of this extract have been thoroughly studied and its limitations rather clearly defined. A method of assay is being perfected so that it appears likely that the product will shortly be made generally available to the medical profession. Improperly used, results may occur of such seriousness as to interfere greatly with establishing the true worth of the product. To secure proper results, a knowledge of scientific dietetics is necessary, and carefully controlled laboratory observations are important. Physicians who plan to use the remedy must inform themselves fully of its potency, the symptoms of danger, the proper methods of administration, the proper methods of antidoting unfavorable effects, and the correct manner of evaluating results. If these precautions are observed, there seems to be no reason why any well-trained physician should not be able to use the remedy satisfactorily."

Among those who declare the insulin treatment a success is Frank A. Vanderlip, financier of New York City.

INTENSIFYING PERFUME OF FLOWERS.

Results presented by Professor Daniel of the University of Rennes before the Paris Academy of Sciences seem to open up a new field of possibilities for perfume makers.

By grafting a shoot of wormwood on a chrysanthemum it was found the odor of the chrysanthemum was greatly intensified. From the seeds of the graft splendid plants were obtained the following year, which produced flowers. Some of the blossoms had powerful perfume, but others were entirely odorless.

July 22nd will mark the centenary of the death of William Bartram. Like his father, John Bartram, the son was an eminent botanist. There is an additional interest because of the meeting of the American Pharmaceutical Association in North Carolina, where William Bartram was for a time engaged in business. This year also marks the sesqui-centennial of the latter's coming to the Carolinas, at the request of Dr. John Fothergill, the famous London physician and botanist, to study and collect the natural products of these States.

PERSONAL AND NEW ITEMS.

Editor C. L. Butchers of the *Australasian Journal of Pharmacy*, and active for many years in the pharmacy and drug interests of Australia, has been elected representative to the International Pharmaceutical Congress. It is hoped that Mr. Butchers, when he comes to the United States during his visit, can be persuaded to attend the meeting of the American Pharmaceutical Association in Asheville.

The pharmacists of Victoria tendered a complimentary "smoker" to Mr. Butchers on the occasion of his departure for London to attend the meetings of the International Pharmaceutical Congress and the British Pharmaceutical Conference as the Australian delegate. President Frank Buckhurst, of the Pharmacy Board, presided, and there was an attendance of about 150 representative pharmacists and the heads of the wholesale drug houses. After Mr. Butchers' health had been drunk, the Chairman presented him with a gold wristlet watch suitably inscribed. In doing so, he referred to the tact, ability, and judgment shown by Mr. Butchers during the twenty-five years he had been connected with Victorian pharmacy. The fact that he was going home as the representative of all the Australian Boards spoke volumes for the esteem in which he was held. Mr. Butchers, in response, said that he appreciated the honor conferred upon him. He would look forward to meeting the big men of pharmacy in Great Britain, and he hoped to return at the end of the year ripened with the experience he had gained and ready to take up his duties again with renewed vigor. The function was a memorable one, and was greatly enjoyed by those present.

James S. Robinson, veteran druggist of Memphis, Tenn., and of the American Pharmaceutical Association, has not been very well for a number of months, necessitating his absence from business.

E. P. Galt, dean of the Alabama Pharmaceutical Association, died following a stroke of paralysis at his home in Selma, Ala., June 17. Dr. Galt was one of the organizers of Alabama Pharmaceutical Association and for thirty-five years served on the Board of Pharmacy. The deceased was 76 years old. His service bespeaks his merit.

Wilhelm Bodeman, John Blocki and Charles Matthews, of Chicago, recently celebrated birthdays. The former and latter divide honors on the same day, June 7, and the occasion was celebrated at the home of Mr. Matthews, where luncheon was served to members of C. V. D. A. under the trees of the spacious grounds.

E. C. Bent, venerable secretary of the South Dakota Pharmaceutical Association, will retire from office after twenty-six years of service.

In token of esteem the students of the South Dakota School of Pharmacy presented Mr. Bent with a beautiful loving cup on May 10. The presentation was enhanced by the presence of many members of the State Association, among them:

President and Mrs. J. C. Shultz, of Madison; Mr. and Mrs. D. F. Jones, of Watertown; A. A. Woodward, of Aberdeen; D. F. Dexter, of Canton; J. A. Pool, of Redfield; E. C. Baldwin, of Rapid City; Professor and Mrs. E. R. Serles, C. D. Kendall, Mrs. Chapman, Professor and Mrs. A. Hogstad, Jr., Professors Morrison and LeBlanc, of Brookings.

Henry C. Christensen, Chicago, **John Coleman,** Wheeling, and **H. Lionel Meredith,** Hagerstown, Md., were honored with the degree of Master in Pharmacy, by the Philadelphia College of Pharmacy and Science, June 6. **J. W. E. Harrisson** was awarded the degree of Master in Pharmacy (in course).

Joseph J. Pfiffner, who earned the Fairchild scholarship in 1922, won all the prizes offered to members of his class in the University of Iowa, School of Pharmacy; these included a set of Britton & Brown's "Illustrated Flora," offered by J. M. Lindley, '89, and three recommendations to membership in the American Pharmaceutical Association, offered by as many donors. Mr. Pfiffner was recently elected to the Rho Chi Society honorary membership fraternity, ranking first among those eligible for election at this time. He expects to continue work in the college next year.

Dr. Robert P. Fischelis has been elected managing editor of the "News Edition" of *Industrial and Engineering Chemistry*, American Chemical Society. He has been a member of the staff of the former for several years. The American Chemical Society profits by his service and best wishes are extended. This will not interfere with his duties as dean of the New Jersey College of Pharmacy.

Reginald E. Dyer, editor of the *Practical Druggist*, completed his twenty-first year of service with that publication on May 25. The publisher of *Practical Druggist*, Romaine Pierson, gave a luncheon at the New York Drug Club, in honor of the celebrant, at which

fifteen guests were present. Brief remarks were made by the guests, expressive of their esteem and the value of the work accomplished by Mr. Dyer. The latter became assistant editor of the *Practical Druggist* in 1903; prior to that time he had been engaged in pharmacy. Mr. Dyer is a graduate of the Montreal College of Pharmacy, class of 1888.

Carson P. Frailey has been elected Secretary of the American Drug Manufacturers' Association, succeeding **A. Homer Smith,** who resigned to affiliate with Sharp & Dohme, Baltimore.

Richard H. Timmermann, New York College of Pharmacy, had the pleasure of presenting a Trustee prize, of $100, to his daughter, a member of the graduating class.

Dean A. Ziefle, of the School of Pharmacy, Oregon Agricultural College, is seeking information relative to the buildings and equipment of other pharmacy schools. A new building is to be erected on the College Campus for the School of Pharmacy.

E. C. Mason, President of the Arizona Pharmaceutical Association, attended the meeting of the Kansas Pharmaceutical Association and will visit other organizations to acquaint himself with these organizations for the benefit of the recently organized association of which he is the president. Mr. Mason owns three stores in the Salt River Valley. He is at the head of the Americanization of the Salt River Valley and president of the Phoenix social service bureau, which has charge of the charities of the city.

D. v. Riesen and wife, of Marysville, Kansas, are visiting in Southern California on a two months' vacation. During the absence of Mr. v. Riesen from his store, his son, Waldemar, assisted by Victor McEntire, will be in charge.

Ellis W. Cookson, druggist of Wichita, Kas., attended the Shrine Convention in Washington, D. C., last month.

Dr. Harvey W. Wiley delivered the Commencement address at Hahnemann Medical College in Philadelphia.

Dr. Edgar Fahs Smith, ex-president of the American Chemical Society, laid the cornerstone of the new chemical laboratory of the Rice Institute, Houston, June 4. The laboratory, which will be erected at an approximate cost of $1,000,000, will be ready for occupancy by the opening of the school in September, 1924.

Hugo H. Schaefer, of the faculty of Columbia University College of Pharmacy, New York, writes that he is at work under Dr. A. Tschirch, University of Bern, and very much pleased with his opportunities. He desires to be remembered to friends and members of the American Pharmaceutical Association.

Dr. John R. Minehart, Dean of Department of Pharmacy in Temple University for the last sixteen years, was the guest of honor at the seventeenth annual banquet of the Alumni Association of the Pharmacy Department. Addresses were made by Dr. Russell H. Conwell, Dr. William Krusen, Dr. Frank Hammond, and others.

Dr. Henry M. Whelpley recently addressed the St. Louis Society of Authors of which he is a member. His subject was "The Artificial Earth Mounds of the United States."

Dean Charles H. LaWall will be the guest of Canada Pharmaceutical Association and address the convention at its next annual meeting.

President Julius A. Koch, of the American Pharmaceutical Association, has appointed **Dean W. F. Rudd** and **W. L. Cliffe** delegates to the Federation Internationale Pharmaceutique, the meeting of which is to be held in London, July 24. The Diamond Jubilee Meeting of the British Pharmaceutical Conference will convene during the same week.

F. E. Mortenson, Pueblo, has been elected president of the Colorado Board of Pharmacy, and **Charles J. Clayton** reëlected secretary.

J. L. Hopkins, president of J. L. Hopkins & Co., has completely recovered from his recent illness and is again presiding at his desk.

Carl Winter, editor of *Association News,* Northern Ohio Druggists' Association, has favored us with the June number of that publication, which contains an editorial addressed to graduates in pharmacy. In this the graduates are impressed with the importance of Association affiliation, and the work accomplished by State and National Associations forcefully presented. A copy of the editorial was given each of the graduates in pharmacy of Western Reserve University, and of Ohio State University.

The Red Cross Messenger reviews the progress made during the past year in promoting publicity for pharmacy, and concludes the editorial with the following paragraph:

"Now the call is for greater coöperation. The campaign will not be a complete success until every druggist falls in with its spirit and every manufacturer of drug store products puts the weight of a publicity campaign be-

hind it. Action, not discussion, must be the program for the coming year."

The Food and Drug Bulletin, of the Department of Health, of New York City, is sent free of charge to all New York City druggists, who by a new regulation, adopted by the Board of Health, are required to keep it on file, and to various food dealers and news agencies concerned with the activities of the Bureau of Food and Drugs.

The Civic and Commercial Journal of the Greenville, S. C., Chamber of Commerce, devoted three pages of its June issue to the joint convention of the South Carolina and North Carolina Pharmaceutical Associations, held in Greenville, June 26–28.

NEW NATIONAL HOME FOR SCIENCE ESTABLISHED IN WASHINGTON.

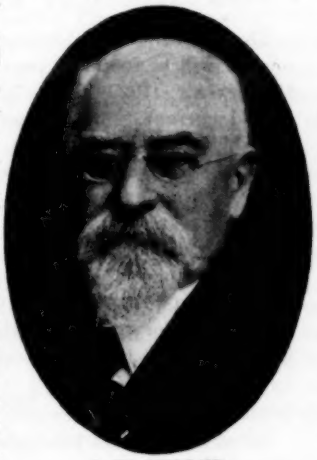
A national home for science and research has been nearly completed in Washington. Not far from the Lincoln Memorial, facing the Mall, this new home of the National Academy of Sciences and the National Research Council, costing $1,500,000, covers a city block containing approximately 189,755 square feet.

Exhibition rooms surround the central rotunda, and in these rooms the latest results of scientific and industrial research will be illustrated. The newest discoveries in all the sciences and their application will be shown in this constantly changing living museum.

OBITUARY.

ADOLPHUS W. MILLER.

Adolphus W. Miller died at his home in Philadelphia July 7, aged 82 years. Reference to the deceased was made in the brief sketches of 50-year members of the A. Ph. A., April JOURNAL, 1919, p. 253; data relating to Dr. Miller's activities are recorded on p. 257 of "First Century of the Philadelphia College of Pharmacy." He graduated in Pharmacy, in 1862; in Medicine, 1871; he received the degree of Ph.D., in 1872, from the University of Pennsylvania, and was a member of the medical faculty for quite a number of years. He was a founder of the Alumni Association, P. C. P., its president in 1875, and corresponding secretary of the college since 1886.



A. W. MILLER.

He was an ardent botanist and actively identified with the management of Bartram's Garden, the Academy of Natural Sciences, the Pennsylvania Botanical Society, and other organizations. He was an ex-president of the Lotus Club; served three terms as president of the Philadelphia Drug Exchange, and as one of its directors for thirty-three years. Dr. Miller's command of language enabled him to convey information interestingly; he was a linguist, and his knowledge of languages included several of the eastern countries.

SOL. A. ECKSTEIN.

Sol. A. Eckstein, druggist and a leading figure in the business circles of Milwaukee, Wis., died in that city early Sunday morning, June 3.

Mr. Eckstein was born in New York City in 1858, and the following year went to Milwaukee, where he was educated. When 16 years old he entered the employ of I. N. Morton, who in 1875 disposed of his drug business to George Wright & Brother. Mr. Eckstein continued with the new firm, which in 1892 was incorporated as the Wright Drug Company. In 1907 he bought out his partners, and became president of the company. A few months ago he disposed of his interests in the latter business.

Mr. Eckstein was a worker in the cause of organized pharmacy, both as a member of the A. Ph. A. and as a vice-president of the N. A. R. D. He had also served two terms as president of the Wisconsin Pharmaceutical Association, and at the time of his death was the head of the Druggists' Mutual Fire Insurance Co. He was also serving his second term as a member of the Milwaukee Park Board, was a director of the American Founders' Security Co., and served three terms as president of the Old Settlers' Club. He was well known in fraternal circles.

He is survived by his widow, his son, Charles, and two brothers, Henry, of Milwaukee, and Louis, of Chicago. Mr. Eckstein joined the American Pharmaceutical Association in 1912.

SOCIETIES AND COLLEGES.

RATES AND ROUTES TO THE ASHEVILLE A. PH. A. MEETING.

Chairman Turner F. Currens, of the A. Ph. A. Transportation Committee, writes that he has made a definite reservation of 35 state-rooms with the Clyde Steamship Co., on the *Arapahoe* scheduled to sail from Pier 36, North River at 12 noon, Daylight Saving Time, August 30.

Quite a number of our members have indicated their intention to go to Asheville from New York via the Clyde Line to Charleston, S. C., and then by train from Charleston to Asheville. The party leaving here August 30, noon, will arrive in Charleston Saturday noon, September 1; leave Charleston Saturday night and arrive in Asheville Sunday afternoon.

The expense of the trip from New York to Charleston, including berth, meals, etc., is $32.95, and $11.05 covers the cost of a ticket and lower berth from Charleston to Asheville. All reservations have been made on the upper or promenade deck. If a more luxurious reservation is desired, there are rooms that can be had at a cost of $5 to $12 in addition to the figures mentioned above.

This trip has the advantage of the two-day ocean voyage, and ample time in Charleston to look over this historical old City, as the guest of our fellow member, Dr. W. H. Zeigler, of Charleston.

Reservations should be made promptly by writing to Turner F. Currens, Chairman, Transportation Committee, A. Ph. A., 55–59 East 11th St., New York City.

ROUND-TRIP SUMMER TOURIST FARES TO ASHEVILLE.

Secretary William B. Day writes that he is informed by the Big Four Railroad that the following round-trip summer tourist fares to Asheville, N. C., are now in effect:

From Champaign, Ill., $35.50; Chicago, Ill., $40.80; Peoria, Ill., $38.65; Indianapolis, Ind., $30.20; Ann Arbor, Mich., $40.35; Detroit, Mich., $39.75; Buffalo, N. Y., $49.84; Cleveland, Ohio, $39.35; Columbus, Ohio, $31.60; Dayton, Ohio, $27.85; Toledo, Ohio, $36.40; Pittsburgh, Pa., $42.65; Charleston, W. Va., $30.70; Cincinnati, Ohio, $24.70; Lafayette Ind., $33.95; Louisville, Ky., $23.50; Milwaukee, Wis., $45.70; Minneapolis, Minn., $59.10; St. Paul, Minn., $59.10; St. Louis, Mo., $26.55.

These summer tourist rates hold from May 15th to September 30th, inclusive, going and return, the final return limit of October 31st offering liberal stop-over privileges on either going, return or both. The Southern Railway System informs us that the round-trip summer rate tickets to Asheville can be secured including side-trip to Chattanooga, Tenn., without additional cost. By taking the side-trip to Chattanooga, Lookout Mountain, Missionary Ridge, Chickamauga Battlefields, Signal Point and Grand Canon of Tennessee can be visited.

Be certain to consult your Railroad Agent early so you will experience no difficulties or disappointments. Hotel rates are quoted in this issue of the JOURNAL, in the article by Local Secretary J. G. Beard, on page 572.

THE SECTIONS OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

The names and addresses of the Section officers will be found on page x, under Official Roster for 1922–1923. Titles of papers should be sent to the officers of the Section for which they are intended, at an early day, so as to enable the officers to prepare the program of the sessions; please do this by the 1st of August. If you can also send in an abstract of your paper, it will be very helpful; this applies also to papers. Copies of papers may be sent to the JOURNAL Office, 253 Bourse Building, prior to the meeting; but the originals should go to the officers of the Sections.

SCIENTIFIC SECTION.

On page 562 of the June issue of the JOURNAL, the officers of the Scientific Section have outlined the program for the Asheville meeting of the A. Ph. A. Please refer to this announcement. The chairman is Dr. Arno Viehoever, Bureau of Chemistry, Washington, D. C. The address of Secretary J. P. Snyder is 32 Elms St., Norwich, N. Y.

SECTION ON PRACTICAL PHARMACY AND DISPENSING.

The Section on Practical Pharmacy and Dispensing asks for your coöperation and requests papers relating to practical and dispensing pharmacy, hospital pharmacy, etc. It is the democratic Section of the Association. It appeals to educators, editors, manufac-

turers, wholesalers, retailers, employers, and employees, alike.

What new ideas have you discovered during the past year? What new thought have you unearthed that might be of service to your fellow-men? Combine them into a paper and present it for discussion in this Section.

Many interesting papers are being prepared for this Section. You should not miss hearing them. What will yours be? Will you again contribute this year as you have so ably done in the past? There is still ample time for this accomplishment.

CROSBY B. WASHBURNE, *Chairman*,
206 Kitchener Ave., Detroit, Mich.
ROBERT J. RUTH, *Secretary*, Elyria, Ohio.

SECTION ON EDUCATION AND LEGISLATION.

The Section on Education and Legislation solicits papers on educational and legislative topics; no subjects are of greater importance and value. Will you discuss in your paper the Model Modern Pharmacy Law or Prerequisite Legislation? Restricted ownership of drug stores to those duly qualified by education and character during these times when efforts are made to undermine the morale of the drug business by those who seek to enter for mercenary reasons chiefly or only—papers on the subject are timely. Many other thoughts for the preparation of papers will present themselves. Secretary G. A. Bergy, Department of Pharmacy, Morgantown, W. Va., and Chairman W. F. Gidley, Purdue University, Lafayette, Ind., will welcome papers dealing with any subject relating to education and legislation. Secretary G. A. Bergy has addressed the deans and members of pharmaceutical faculties as follows:

"The Section on Education and Legislation of the American Pharmaceutical Association is at this time urging you and the various members of your staff to prepare papers on those phases of pharmaceutical education and legislation in which they are most deeply interested.

"The question of uniform college entrance requirements and a year of college training as a prerequisite is to-day commanding much attention.

"The legislatures of the various states have recently enacted many laws, perhaps many concerning pharmacy. What has been the progress in your state? State specifically in the summary of your report the qualifications necessary for the practice of pharmacy in your commonwealth.

The secretary of the Section is very desirous of learning the title of your paper in order that the programs may be completed at the earliest possible date."

SECTION ON COMMERCIAL INTERESTS.

No Section offers opportunities for a larger number of contributors than the Section on Commercial Interests. The Business Side of Pharmacy is ably presented in each issue of the JOURNAL by Dr. Robert P. Fischelis. Business Management, management of the sales department, profits, over-head expenses, items that may be successfully handled in pharmacies and drug stores, the prescription department, pricing of prescriptions, keeping records, stock records, etc., are all subjects that concern pharmacists and druggists every day. Exchange your views with others. Papers should be mailed to Chairman Walter M. Chase, P. O. Box 484, Detroit, Mich., or Secretary Henry B. Smith, 291 So. 5th St., Brooklyn, N. Y.

SECTION ON HISTORICAL PHARMACY.

The principal work undertaken by the Section on Historical Pharmacy is the preparation of a history of American Pharmacy. Other historical papers will, however, be welcomed and contributions should be mailed to Chairman Clyde L. Eddy, 100 William Street, New York City, Secretary Robert S. Lehman, 375 3rd Ave., New York City, or the historian, E. G. Eberle, 253 Bourse Building, Philadelphia, Pa. Photographs, books and other historical matter for filing in the Section on Historical Pharmacy should be sent to the latter. If it is your intention that such presentations should be exhibited they may be turned over to the historian at the Asheville meeting.

WOMEN'S SECTION.

The chairman of the Women's Section is Mrs. Lyman F. Kebler, 1322 Park Road, Washington, D. C., and the secretary is Miss Anna G. Bagley, 2423 Indiana Ave., Columbus, Ohio. Papers relating to subjects for the Women's Section should be mailed to the officers.

As has been indicated elsewhere, if it is not possible to send in papers before August 1, the officers of the respective Sections should

be informed relative to the titles of the papers and, preferably, abstracts of the papers should accompany the communications.

The program must be printed in advance of the meeting and the officers will be aided by early responses.

REPORT OF THE DELEGATE OF THE AMERICAN PHARMACEUTICAL ASSOCIATION TO THE PROPRIETARY ASSOCIATION OF AMERICA.

In accordance with instructions, the undersigned appeared as delegate from the American Pharmaceutical Association to extend greetings to the Proprietary Association, which held its 41st annual meeting at the Pennsylvania Hotel, New York City, May 22 and 23, 1923.

The attendance at this convention was 200 or more. Sessions were held both morning and afternoon of each day, and reports were heard from the Requirements Committee, Legislative Committee, Foreign Trade Committee, Membership Committee and the General Counsel.

Frank A. Blair, president for several years, refused to reconsider reëlection on account of the press of new duties. Dr. V. Mott Pierce, Buffalo, was elected to succeed Mr. Blair, who, however, remained on the Executive Committee.

Other officers were elected as follows: *First Vice-President*, E. K. Hyde, New York; *Second Vice-President*, James A. Howe, St. Louis; *Secretary-Treasurer*, Charles P. Tyrrell, Syracuse, N. Y.; *Executive Committee:* R. R. Land, Binghamton, N. Y.; Frank A. Blair, New York; Carl J. Balliett, Greensboro, N. C.; and J. A. Mitchell, New York.

In his annual address, President Blair said that "in spite of the fact that nearly every State legislature in the United States has been in session at some time during the past year, not one single State measure has been passed thus far which is detrimental to the interests of the manufacturer of proprietary articles. Of some four hundred bills affecting proprietary medicines which have been introduced into some forty-odd State law-making bodies at their last sessions, all except one have been defeated, and the passage of this one is not yet assured. Practically all the legislatures have completed their sessions and adjourned for 1923."

E. F. Kemp reported for the Requirements Committee that 112 new preparations had been examined during the year and that eight new members had been admitted to the organization. The report of the Legislative Committee was made by Chairman W. E. Weiss. Mr. Weiss reviewed the work of his committee during the year and discussed legislation now pending. Harry B. Thompson, *General Counsel*, read an exhaustive report of his activities during the year. The report of the Foreign Trade Committee was read by Chairman J. A. Mitchell, and Chairman Stanley P. Jadwin, of the Membership Committee, made his report.

Henry Miles, a member of the Canadian Parliament and representing the P. A. T. A. of Canada, spoke upon the sales tax now in effect in that country and of recent legislation regulating the sale of proprietary medicines.

CHARLES W. PARSONS.

MEMBERSHIP PRIZES OF SCHOOLS AND COLLEGES OF PHARMACY IN THE AMERICAN PHARMACEUTICAL ASSOCIATION.

Mention has been made in a previous issue of the JOURNAL of awards of membership to graduates. Other awards follow, and mention will be made in succeeding numbers, provided the JOURNAL receives the necessary information, for which thanks are extended. Brooklyn College made two awards, through Dean William C. Anderson, to I. B. Facton and H. J. Kleinfeld.

Fordham awarded membership to William Sandler, reported by Dean Jacob Diner.

The William Gray Membership Prize, of Illinois University School of Pharmacy, was awarded to Charles E. Rutledge; the prize in Materia Medica was given to Harold B. Reinhart, and for Chemistry to Cyril E. Tokarski.

Mention has been made of the awards to Joseph J. Pfiffner, of the College of Pharmacy, University of Iowa, and a subscription to the JOURNAL A. PH. A. was awarded to Sister Mary Catherine by Prof. R. A. Kuever, for highest rank in the first year practical pharmacy.

Dean Robert P. Fischelis, New Jersey College of Pharmacy, made two awards; for the highest average in pharmacy to Arthur Harry Adelmann, and to Charles Keppler, Jr., for highest average in commercial pharmacy.

The pharmacy review prize of the Philadelphia College of Pharmacy and Science was awarded to Bernard Albert.

Pittsburgh College of Pharmacy made the following awards: Theoretical pharmacy prize to E. Frederick Rowse; chemistry prize to Joseph Stein; pharmaceutical products prize to Ralph Hite; pharmacognosy prize to Edward Labowitz, and for materia medica to Sidney Odle.

STATE PHARMACEUTICAL ASSOCIATIONS.

At this writing all advices indicate that there has been a general approval of the reorganization plan of the American Pharmaceutical Association by State associations. Action has also been taken by many associations for contributions to the A. Ph. A. Headquarters Fund. The Minnesota State Pharmaceutical Association made a contribution of $500, which has been reported. Under the direction of President Samuel L. Antonow, other officers, the executive committee and members of the Illinois Pharmaceutical Association, nearly $3000 was pledged by members for the fund. The meeting of the latter association was held on Lake Steamer, South American, on a four-day cruise on the Great Lakes.

OFFICERS OF STATE PHARMACEUTICAL ASSOCIATIONS 1923–1924.

(Secretaries of associations are asked to make corrections and send in list of officers, and names of next convention city.)

ALABAMA.

President, R. F. Lovelady, Birmingham.
First Vice-President, E. C. Fowler, Montgomery.
Second Vice-President, Claude Hagan, Birmingham.
Treasurer, S. L. Toomer, Auburn.
Secretary, W. E. Bingham, Tuscaloosa.
Auburn was selected as the 1924 convention city.

DELAWARE.

President to be chosen by the directors.
Vice-Presidents, George W. Brittingham, New Castle; Harry P. Jones, Smyrna.
Treasurer, Peter T. Bienkowski, Wilmington.
Directors, O. C. Draper, F. E. Gallagher, Charles E. Young, Joseph S. Brokaw, N. B. Danforth, all of Wilmington.

ILLINOIS.

The Illinois Association, as an organization, contributed $500 to the A. Ph. A. Headquarters Fund. President S. L. Antonow and W. D. Duncan subscribed $500 each, and the total subscribed amounted to nearly $3000.

President, J. P. Crowley, Chicago.
First Vice-President, P. L. Pfaff, Centralia.
Second Vice-President, L. H. Pedigo, Chicago.
Third Vice-President, J. B. Nuchels, El Paso.
Secretary, W. B. Day, Chicago.
Treasurer, George M. Bennett, Urbana.
Arrangements for the next place of meeting were left to the Executive Committee.

KANSAS.

President, F. A. Milne, Pratt.
First Vice-President, F. M. Arbuthnot, Belleville.
Second Vice-President, Charles W. Browne, Chanute.
Treasurer, John Schmitter, Gypsum.
Secretary-Manager, J. Will Kelley, Topeka.
Topeka was chosen as the place for the 1924 meeting.

MARYLAND.

Plans were inaugurated for the affiliation of District of Columbia pharmacists with the Maryland Association. Approval was given to the policies of the University of Maryland to develop a great State University.
President, Charles L. Meyer, Baltimore.
First Vice-President, W. K. Edwards, Cumberland.
Second Vice-President, H. A. B. Dunning, Baltimore.
Third Vice-President, John H. Farlow, Berlin.
Secretary, E. F. Kelly, Baltimore.
Treasurer, Samuel Y. Harris, Baltimore.
An amendment was adopted creating the office of assistant secretary, who will devote all of his time to the office. Secretary Jeannot Hostmann of New Jersey Pharmaceutical Association attended the sessions and was one of the speakers.

MASSACHUSETTS.

President, Fred E. Jones, Lowell.
First Vice-President, C. Fred Wright, Boston.
Second Vice-President, Maurice W. Corbin, Worcester.
Secretary, James F. Guerin, Worcester.
Treasurer, John J. Tobin, Boston.

MICHIGAN.

Resolutions of importance were adopted which are reported under the Department of the American Conference of Pharmaceutical Faculties.
President, D. D. Alton, Fremont.
First Vice-President, Milo Bolender, Sparta.
Second Vice-President, L. E. Chandler,

Charlotte.

Secretary, Louis V. Middleton, Grand Rapids.

Treasurer, A. De Kruif, Zeeland.

Members of Executive Committee: John G. Steketee, Grand Rapids, and Ellis E. Faulkner, Middleville.

Member Prescott Memorial Scholarship Association, Charles H. Stocking.

Selection of 1924 meeting place was left to the Executive Committee.

MISSOURI.

President, Fred H. Fricke, St. Louis.

Honorary President, Samuel Farrar, Lebanon.

First Vice-President, Arthur Schulte, St. Louis.

Second Vice-President, T. H. Nelson, St. Joseph.

Third Vice-President, Robert Lisch, Springfield.

Treasurer, William Mittelbach, Boonville.

Secretary, C. C. Payne, Kansas City.

Assistant Secretary, Harry Pierce, Kansas City.

Historian, H. M. Whelpley, St. Louis.

Springfield was chosen as the place for the 1924 meeting.

NEW JERSEY.

Recommendations to issue a monthly bulletin and organize county organizations were adopted. Dr. R. A. Lyman of Nebraska, Dr. A. G. DuMez of Washington, and E. F. Kelly of Baltimore were among the speakers of the convention.

President, Daniel H. Hills, Spring Lake Beach.

First Vice-President, L. L. Staehle, Newark.

Second Vice-President, Robert P. Fischelis, Newark.

Secretary, Jeannot Hostmann, Hoboken.

Treasurer, Edgar R. Sparks, Burlington.

Board of Trustees: Luke C. Hines, Thomas K. Edwards, C. J. McCloskey, Harry J. Quin, Henry Schmidt, Jeannot Hostmann and Danel H. Hills.

New Jersey now has a law that empowers the State Board of Pharmacy to suspend as well as revoke the certificate of registration of members twice violating the pharmacy law, the act referring to the sale of liquor and the narcotic act.

Lake Hopatcong was chosen as the place for the 1924 meeting.

NEW YORK.

Hearty approval was given to the law recently enacted limiting ownership of drug stores to licensed pharmacists. Steps will be taken to reorganize the State Association for more effective legislative work.

President, Emory H. Breckon, Buffalo.

First Vice-President, George R. Christ, Brooklyn.

Second Vice-President, T. Bruce Furnival, Syracuse.

Third Vice-President, Herman Walter, New York.

Secretary, Edward S. Dawson, Syracuse.

Treasurer, Frank Richardson, Cambridge.

Members of the Executive Committee: Pincus Herz, New York; W. R. Tongue, Poughkeepsie, and John Scavo, New York.

PENNSYLVANIA.

President Harlan J. Mentzer presented a number of important recommendations in his address; as a result the *Pennsylvania Pharmacist* is to be issued quarterly; the services of the Pennsylvania Board of Pharmacy were endorsed, and resolutions thereon sent to the Governor. Resolutions were adopted relating to sale of alcohol, and also that members convicted of illegal sales may be expelled from the association.

President, P. Henry Utech, Meadville.

First Vice-President, William E. Cline, Philadelphia.

Second Vice-President, Clarence Croft, Waynesboro.

Secretary, Louis Saalbach, Pittsburgh.

Treasurer, F. H. E. Gleim, Lebanon.

Local Secretary, George D. Kressler, Bethlehem.

Executive Committee: W. J. Sturgeon, J. C. Peacock, Harlan J. Mentzer.

Bethlehem was chosen as the place for the 1924 meeting.

TEXAS.

A feature of the meeting was the Drug Show, to which about forty exhibitors contributed.

President, W. H. Wentland, Manor.

President-elect, W. H. Whisenant, San Antonio.

First Vice-President, D. Scott Keene, Galveston.

Home Secretary, J. W. Graham, Austin.

Historian, Miss Lum Shipe, San Marcos.

Secretary-Treasurer, Walter D. Adams, Forney.

Selection of the place for the 1924 meeting was left to the Executive Committee.

OFFICERS OF NATIONAL ASSOCIATION OF DRUG CLERKS.

President, Arthur M. Turitt, Charleston, W. Va. *First Vice-President*, Otto E. Bruder, Palmyra, Wis. *Second Vice-President*, Carl J. Nastoupil, Sealy, Tex. *Secretary-Treasurer*, Paul J. Mandabach, *Counsellor-at-Law*, R. A. Cavanagh.

THE PHARMACIST AND THE LAW.

GOVERNMENT IS CHANGING FROM A REPRESENTATIVE TO A BUREAUCRATIC FORM.

Congressman Hatton W. Sumners of Texas recently said:

"Perhaps the most important thing which has ever happened in the history of any important government, unless a change is brought about by a revolution, is the change which is taking place in the functioning machinery of the National Government.

"Without a modification of our Constitution, without any formal act whatever, the National Government is rapidly changing from a representative government to a bureaucratic government. This change is resulting from the fact that the share of general governmental responsibility which has been transferred to the Federal Government exceeds the capacity of any representative government to discharge.

"The result is that resort is had to bureaus which, insofar as their practical operation is concerned, combine in themselves legislative, executive and judicial powers. That is, they promulgate rules and regulations, construe them and assess penalties.

"No member of Congress favors this change. It is resulting from the limitation which nature puts upon human capacity. It is impossible for the members of Congress, with our vast territory, population, diversity of interests, to formulate an independent judgment with regard to important governmental matters of the most vital interest to the people. As a result, bureaus are created to which general grants of power are made which include the power to make rules and regulations and to enforce them.

"Some of those who founded the Government were apprehensive that governmental power would be absorbed by the Federal Government, but they never dreamed that the people of the States would themselves initiate the transfer of that power to the Federal Government. It has been a surrender and not an absorption.

"Lying at the bottom of the whole difficulty, of course, is the mistaken notion which the people of the country seem to have gotten in comparatively recent years as to the efficiency of laws enacted by legislative agencies."

200,000 LAWS ANNUALLY ENACTED IN UNITED STATES.

Year in and year out an average of 10,000 new laws are annually enacted by Congress and the several State legislatures in response to the American passion for law-making, according to an article in the May issue of "*The Budget*," the monthly publication of the National Budget Committee, by William P. Helm, Jr., its Washington correspondent. In addition to the Federal and State law-making bodies there are city, town and county councils meeting regularly to the number of more than 15,000; and upwards of 3,000 county legislatures. Allowing an average of only ten laws or ordinances a year for these bodies, the writer estimates that as a nation we enact each year more than 200,000 legislative measures applying to the various jurisdictions.

The drug business and pharmacy come in for a share of this legislation, which adds not only to enforcement expenditures but also to the overhead expenses of druggists and pharmacists.

THE WARNER AND MENNEN PRICE PLANS.

The Federal Trade Commissioner has issued a formal complaint against Wm. R. Warner & Co., Inc., alleging unfair competition and price discrimination. The *Oil, Paint and Drug Reporter* comments:

"It is noted that the nature of the price discrimination presented in the Warner case is different from that presented in the Mennen case. In the Mennen case the discrimination was in favor of wholesalers as against retailers purchasing coöperatively. In the Warner case the discrimination alleged to be in use is in favor of a preferred class as against a non-preferred class, the preferred class including both wholesalers and retailers and the non-preferred class also including both wholesalers and retailers.

"In the Mennen case the commission's order prohibited a discrimination against retailers purchasing coöperatively upon the same terms as wholesalers. The court reversed the order and stated:

"Whether a buyer is a wholesaler or not does not depend upon the quantity he buys. It is not the character of his buying, but the character of his selling which marks him as a wholesaler. . . .'

"The question in the Warner case to be determined by the commission is whether it is unlawful to discriminate in price between wholesalers who purchase in the same quality, quantity and upon the same terms, and likewise, whether it is unlawful to discriminate between retailers who purchase under like conditions."

MANUFACTURERS MAY ESTABLISH WHOLESALE AND RETAIL PRICE LISTS AND MAY CLASSIFY THEIR CUSTOMERS ON A BASIS OF CHARACTER OF BUSINESS.

The United States Supreme Court on Monday, June 11, 1923, denied the application of the Federal Trade Commission for a review of the decision of the United States Circuit Court of Appeals, Second Circuit, in the case of Federal Trade Commission vs. Mennen Company.

A comment from "Bulletin No. 74" of the Wholesale Druggists' Association follows:

"This decision by the United States Supreme Court establishes clearly the following rights of a manufacturer engaged in a wholly private business, in the absence of any intention to create a monopoly, or of a combination or conspiracy with any other party:

"1. The right to sell only to individuals, firms or corporations of his own selection, and to decline to sell to all others for any reason or for no reason. He may sell only to wholesalers, or he may sell only to retailers, or he may sell to both wholesalers and retailers.

"2. The right to establish and announce list prices for wholesalers and different list prices for retailers.

"3. The right to classify customers as wholesalers or as retailers on the basis of the character of their selling, regardless of quantity purchased.

"The decision does not give the right to a group or association of manufacturers to adopt in combination a sales policy similar to that of the Mennen Company, or to a group or association of dealers the right to coerce manufacturers into adopting such a sales policy. It likewise gives no right to a group or association of dealers to coerce manufacturers to abandon the Mennen or a similar sales policy and to adopt one based on quantity price schedules.

"What every wholesale druggist and every manufacturer should clearly understand is that a manufacturer by his own individual voluntary action may vary his schedule of prices and may establish wholesale prices and retail prices, allowing wholesale prices only to wholesalers of his own selection and charging retail prices to all retailers regardless of the quantity purchased."

RETAIL DRUGGISTS' AND HOSPITAL LIQUOR ALLOWANCES.

Below are printed rules that have been set forth in Pro-Mim 221 issued by Prohibition Commissioner Haynes regarding the procurement and allowance of liquor supplies for retail druggists and hospitals.

1. The basic permit fixes the quantity which may be procured yearly or quarterly by retail druggists and hospitals.

2. Retail druggists and hospital permittees shall be permitted to procure the full amount fixed by their basic permit, and no Director or other officer shall reduce the amount so procurable when applied for, except upon satisfactory proof that it is more than is needed for legitimate use, and no Director or other officer shall make any reduction of this allowance without first giving the permittee an opportunity to appear in person, or by attorney, or submit a statement in writing, giving his reasons why he should have the amount applied for, and a reasonable time shall be given permittee to supply this information.

3. When a permittee shall not use this entire quarterly allowance within a given quarter such residue shall not be deducted from his allowance for subsequent quarters, and he shall be entitled to withdraw during the year an amount equal to his aggregate quarterly allowance.

4. In passing upon the renewal applications of retail druggists and hospitals, previous allowances thereunder will be authorized without delay or question, unless the Director is in possession of proof sufficient to warrant the inquiry provided for in the preceding paragraph.

5. As the needs of hospitals are usually imperative, their applications should be subjected to as little delay as possible and should have priority of consideration.

6. These instructions shall be construed and applied with a view of allowing retail druggists and hospitals such quantities of liquors as are required to meet their legitimate demands, and action thereon shall be expedited as far as is practicable.

TREASURY DECISION 3480.

Prohibition—Certain basic permits to be issued by directors—Certain applications to be approved without investigation.

Modification of Article III, Regulations No. 60, as amended by T. D. 3398.

TREASURY DEPARTMENT,
Office of Commissioner of Internal Revenue,
Washington, D. C.

To Federal Prohibition Directors and Others Concerned:

1. Directors are hereby vested with the same authority as that given the commissioner by Article III of Regulations No. 60, as amended by T. D. 3398 to approve or disapprove applications for and to issue the following basic permits:

(1) Permits to physicians to prescribe;
(2) Permits to physicians to use intoxicating liquor;
(3) Permits to dentists and veterinarians to use alcohol;
(4) Permits to transport by truck; and the procedure relating to such applications and permits will correspond with that relating to basic permits issued by the commissioner.

2. Applications on Form 1404 may be acted upon by the director without making inspection, where the director has evidence justifying his action without inspection.

3. T. D. 3288 and T. D. 3395 are in no way affected by the foregoing, and applications for increased quantities of liquor and for additional books of prescription blanks will be forwarded to and acted upon by the commissioner as heretofore.

D. H. BLAIR,
Commissioner of Internal Revenue.

Approved May 18, 1923:
A. W. MELLON,
Secretary of the Treasury.

BOOK NOTICES AND REVIEWS.

The Year Book of the American Pharmaceutical Association, 1921. Volume 10. Containing the Sixty-fourth Annual Report on the Progress of Pharmacy, and the Constitution, By-Laws, Roll of Members, and Report of the Treasurer, A. Ph. A. Frontispiece, Samuel L. Hilton, President A. Ph. A., 1921–1922. Corresponding to Volume Sixty-nine of the former Proceedings of the A. Ph. A. Cloth. Published by the American Pharmaceutical Association, Chicago, 1923.

The Introductory of the volume by the present Reporter on the Progress of Pharmacy, Dr. A. G. DuMez, gives full credit to Professor Henry V. Arny and his collaborators for the completeness and excellence of the Report; the former edited the manuscript and participated in the preparation of the volume, as one of the collaborators—the others being: Charles W. Ballard, Clarence M. Brown, Lewis N. Brown, Henry M. Burlage, Otto Canis, Zada M. Cooper, May O'C. Davis, William B. Day, George C. Diekman, Herman Engelhardt, Ralph R. Foran, Chester G. Fuss, Edmund N. Gathercoal, Ernest H. Grant, Fanchon Hart, Bruno E. Höckert, Jeannot Hostmann, William J. Macsata, Harold McAdams, E. C. L. Miller, William A. Puckner, Hugo H. Schaefer, Clyde M. Snow, Curt P. Wimmer, Heber W. Youngken.

The abstracts are drawn from the pharmaceutical literature, not only from American publications but from all parts of the world. The subjects have been chosen with judgment of the needs of the pharmacists, representative of the various pharmaceutical activities, and designed to keep pharmacists fully acquainted with the technical side of their calling.

Several years ago an educator declared that a large proportion of the queries he is called upon to answer for students and pharmacists can be answered most satisfactorily by referring to the YEAR BOOKS of the American Pharmaceutical Association. Each subject quotes the publication from which the articles abstracted are taken, so that when necessary the original contribution may be consulted. The Bibliography of Pharmaceutical Research, published in the JOURNAL A. PH. A., indicates the abstracts printed in the YEAR BOOKS.

The general divisions of the YEAR BOOK are classified into subjects under Pharmacy, Materia Medica, Inorganic Chemistry and Organic Chemistry.

Pharmacy is subdivided into general subjects which deal with pharmacopœias, formularies, legislation, laws pertaining to the drug business, associations and colleges. Another section takes up apparatus and manipulations, while the third division relates to preparations, and the last relates to new remedies and trade-named preparations.

In this connection it may be stated that under Pharmacy—apparatus, manipulations and preparations—there are about 300 abstracts and about 600 new remedies are noted. A number of abstracts are accompanied by illustrations; certainly most valuable references for pharmacists.

The abstracts of Materia Medica are divided into general subjects, vegetable drugs, animal drugs, and products. Inorganic subjects are considered under non-metallic elements and metals. Organic Chemistry is treated under the following heads: Volatile oils and derivatives; alcohols and derivatives; aromatic derivatives; fixed oils and fats; carbohydrates; organic acids; organic bases; glucosides and neutral principles; coloring matters; albumenoids; proteins; ferments and enzymes; sera and vaccines; urine, blood and bile compounds; tests, etc.

A reviewer of a former volume of the YEAR BOOK said:

"For the laboratory worker, teacher and scientist, the book is indispensable and has always been so considered. For the busy pharmacist who has little time to more than 'skip' through his journals as they come in from time to time, the YEAR BOOK is an important asset, as the Reporter on the Progress of Pharmacy acts as a *Reading Editor* for him, culling out the essentials from the non-essentials and giving him necessary references in case he wants to look up the originals."

The volume of the YEAR BOOK under discussion, which has recently been published, contains 552 pages of reports, about 1600 abstracts, and the total number of items is over two thousand, requiring 24 two-column pages for listing them, and there is also an index of authors.

For the information of those who desire to purchase a copy of the YEAR BOOK, this issue, as well as preceding volumes, may be obtained by addressing Secretary William B. Day, 701 So. Wood St., Chicago, Ill. The price is $4.00 per volume. The annual Association membership fee includes a volume of the YEAR BOOK.

Dental Formulary. A practical guide for the preparation of chemical and technical compounds and accessories as used in the office and laboratory by the dental practitioner, with an index to oral diseases and their treatment. By Hermann Prinz, A.M., D.D.S., M.D., Professor of Materia Medica and Therapeutics at the Thomas W. Evans Museum and Dental Institute, School of Dentistry, University of Pennsylvania, Philadelphia, Pa. Third Edition, thoroughly revised. 328 pages. Published by Lea & Febiger, Philadelphia and New York. Price, $3.50.

The importance of proper care of the teeth and the fact that many diseases are developed because of lack of attention, and that pharmacists prepare and sell preparations for cleansing the teeth, mouth-washes, etc., prompts a review of this valuable book in these pages. Pharmacists supply dentists and there has always been coöperation between the professions represented; in more recent years this coöperation has contributed a valuable service to the public, and a source of mutual benefit.

The author is well and favorably known and in the *Dental Formulary* has presented formulas which have been shown to have real merit and are worthy of an extended trial at the hands of the profession. Each formula represents a basic compound and may be employed as such or modified to suit the needs; they represent the practical experience of minds who are known as experts in their respective branches.

The book is divided into chapters, thus plaster of Paris preparations, separating media, bases and cast inlays, moulding materials, etc., are first considered. Then guttapercha preparations, plastic impression compounds, etc. Chapters on cements, varnishes, alloys and fluxes follow. A chapter deals with preparations for the mouth and teeth and another relates to pharmaceutical compounds.

Under powders, pastes and washes containing soluble drugs in solution, the author states that "these are employed for the avowed purposes of assisting Nature in accomplishing the desired means to an end, *i. e.*, they must favor the recovery of an inflamed mucous membrane and they must mechanically remove the accumulated food debris." The properties of various oral preparations are

described. There are sixty or more pages of formulas in the chapters mentioned, and the information given is of value to pharmacists. The hundred or more pages following relate to oral diseases, treatment, etc., and contain many formulas, and tests for albumin, sugar, indican, etc., are given. A number of pages outline urine analysis and saliva analysis.

The chapter on miscellaneous subjects includes formulas for toothache gum, toothache drops, lotions, lubricants, plastic compounds, hardening fluids, bleaching compounds, formulas for making negatives, lantern slides and Roentgen-Ray work, etc.

The book will prove of value to pharmacists because the formulas will enable them to supply preparations that have been employed successfully in dental practice, and give them a better understanding of the dentist's needs.

Organic Chemistry or Chemistry of the Carbon Compounds. By Victor von Richter. Edited by Prof. R. Anschütz and Dr. H. Meerwein. Translated from the 11th German edition by E. E. Fournier D'Albe, D.Sc., A.R.C.Sc. Volume III. Heterocyclic Compounds. P. Blakiston's Son and Company. Philadelphia. Price $6.00.

Richter's "Organic Chemistry" needs no introduction to organic chemists. Volume III completes the English translation of the 11th German edition. This volume deals with the heterocyclic compounds having rings containing successively O, S and N, two N members, an O and an N member, and three, four, five, and six-member substances. All except the more rare classes of heterocyclic compounds are considered. The vegetable alkaloids of the pyridine, tropine, cinchonine, morphine and isoquinoline groups are treated in a fairly comprehensive manner from the viewpoint of structure. The information given, however, is not sufficiently comprehensive to fill the requirements of the analyst. The facts stated are so numerous and the subject matter so condensed that the work is much more nearly an encyclopedia than a textbook. Structural formulas are given for the principal representatives of the more important classes of substances. References to the original literature are given quite generally so that the book becomes useful to researchers, particularly those who do not care to purchase the much more expensive works like Beilstein's "Organische Chemie." English-speaking chemists will notice the absence of the year in the references, the volume and page only being given. Another feature particularly unfortunate for the pharmacist is that the last German edition appeared ten years ago. Consequently there are many recently discovered synthetics much used in medicine, such as acriflavine, butyn and mercurochrome, which are not described. Like the preceding volumes in the set, Volume III has its own index. Teachers and students alike will appreciate the resultant increased utility for rapid reference work. Considering the great typographical difficulties in publishing a work so complex as this, the translator and the publisher are to be congratulated on producing a book so free from errors. L. E. WARREN

Jahrbuch der angewandten Naturwissenschaften. Vol. 32, 1920–1921. Von Dr. August Schlatterer. Lex. 393 pp. Cloth, $1.50. Herder & Co., Preiburg in Breisgau.

Germany is the home of the year books. The one before us deals with the entire field of applied natural sciences. Among the many chapters we must call attention to the following which are of special interest to pharmacist, chemist and physician: Chemical Technology by Prof. Dr. Karl Scheid, Dentistry by Dr. Heinrich Lauer, Veterinary Medicine by Dr. K. Brueggemann, and Medicine by Generaloberarzt Dr. Karl von Schnizer. The last subject is cleverly divided into physiology and pathology, general and special therapy and hygiene. This chapter also contains a list of the newer remedies comprising two and a half pages.

Prof. R. Lais in Triberg contributes a special article on "Modern Plant Variation," illustrated with a colored plate showing how dandelion flowers can be varied according to Mendel's Law. This article alone is worth the price of the book! Another valuable addition is the Necrology containing obituaries of scientists, etc., who died during 1920.

The Jahrbuch, or still better, a set of these Year Books, is a valuable addition to any library.

Taschenbuch der Mikroskopischen Technik. Von Benno Romeiss. 10. edition von Alexander Bohm und Albert Oppel. 12 mo. 472 pp. R. Oldenbourg Verlag, München.

If a book passes through ten editions, then it is a proof of its utility. The General Part contains 13 chapters treating the microscope, the microtome and the preparation of the object. The Special Part consists of 22 chapters treating the cell and the microscopical examination of all the different parts of the anatomy including blood and urine.

Very complete indices of Literature, Authors and Subjects conclude this valuable book which we can highly recommend to those interested.

OTTO RAUBENHEIMER, PH.M.

The Riddle of the Rhine. By Victor Lefebure. Victor Lefebure was a French chemical liason officer during the war; in this book he gives a comprehensive description of the development of chemical warfare, from the first use of gas by the Germans in 1915 to the last campaigns of the war. The account of the change, of the releasing of gas from cylinders, to the use of the "Livens Projector" and the German "cross shells" containing gaseous compounds of phosphorus, arsenic and organic poisons, is most interesting.

The book is of the propaganda type, and has for its chief purpose the calling to the world's attention the monopoly of the organic chemical industry which is controlled by the Interessen Gemeinschaft, "I. G.," of Germany. These huge dye works centered along the Rhine and its tributaries put Germany, although technically disarmed, in command of the largest source of munitions the world has ever produced. The connection between organic chemical research in Germany and the government is inseparable and it is estimated that within six days from the outbreak of any future war, Germany would be in a position to control the world supply of dyes, explosives, poisonous gases and organic drugs.

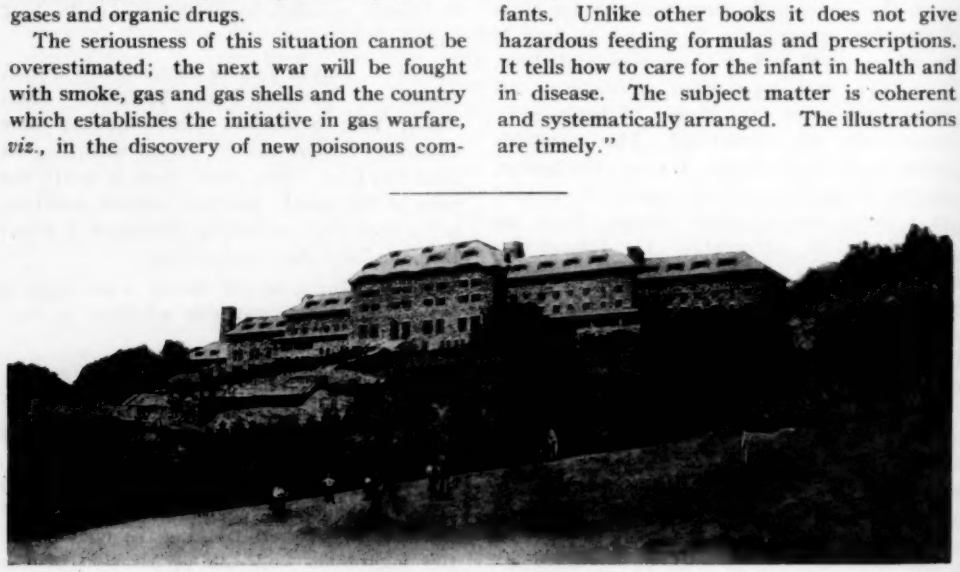
The seriousness of this situation cannot be overestimated; the next war will be fought with smoke, gas and gas shells and the country which establishes the initiative in gas warfare, *viz.*, in the discovery of new poisonous compounds and effective methods of protection, will have on its side one of the greatest components of victory. The treaty of Versailles does not prohibit Germany's taking the lead in the chemical industry and consequently this scientific nation is "fixing" tons of atmospheric nitrogen monthly and establishing an economic system of resources through chemistry, which will stand out as the peer of any country in the world.

Every American interested in the preservation of peace and democracy should read Victor Lefebure's book. The position of the American Chemical Warfare Service and its power and effectiveness in conflict is discussed most judiciously. Finally, the future of any nation in war or in peace is limited by the size of its chemical industries; let us of America build and utilize this fundamental science in industry until researches and power of production of American Chemistry will be the glory of our nation, anything short of this is anachronism in industry.

J. C. KRANTZ, JR.

Nursery Guide for Mothers and Nurses, by Louis W. Sauer, M.D., senior attending pediatrichian, Evanston Hospital, Illinois. Published by C. V. Mosby Company, St. Louis, Mo. Price $1.75. 188 pages.

"This little *vade mecum*, written for mothers and nurses, gives in clear, concise form all essential details in the care and feeding of infants. Unlike other books it does not give hazardous feeding formulas and prescriptions. It tells how to care for the infant in health and in disease. The subject matter is coherent and systematically arranged. The illustrations are timely."



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